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CLINICAL IMMUNITY IN POLIOMYELITIS

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IT IS common teaching that an attack of poliomyelitis confers an immunity which is sufficient to protect a person against subsequent infection. The evidence supporting this view is rarely questioned, for second attacks of the disease are infrequent and antibodies against the virus can be demonstrated in the blood of both human and animal subjects. Antibodies can also be detected in the blood in such a large proportion of the population that it is often concluded that most adults have probably been in contact with the virus without development of recognizable symptoms but nevertheless with acquisition of some degree of immunity. The fact that the most susceptible age group consists of young children for whom the chance of previous immunizing exposure has been minimal also suggests the likelihood of some form of acquired immunity in the population at large. In spite of the evidence indicating immunity to be present after an attack of poliomyelitis, several facts are at hand which raise questions concerning the reliability of the conclusions which are often reached.

The number of second attacks of poliomyelitis reported in the literature is small, only 31 having been found in addition to those presented here.[1] In 1935, Fischer and Stillerman[1a] reviewed the cases and discussed the question of acquired immunity. They could demonstrate no significant difference between the incidence of the disease in the population as a whole and the expected number of persons in that population who had had the disease previously. In 1943, Nelson and Green[1c] came to a simi-

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1. (*a*) Fischer, A. E., and Stillerman, M.: Does an Attack of Acute Anterior Poliomyelitis Confer Adequate Immunity? J. A. M. A. **110**:569-572 (Feb. 19) 1938. (*b*) Halliday, C. H.: Poliomyelitis Situation in Maryland, Bull. Maryland State Health Dept. **13**:77-92 (Nov.) 1941. (*c*) Nelson, N. B., and Green, W. T.: Second Attacks of Anterior Poliomyelitis: Report of Four Cases, Am. J. Dis. Child. **65**: 757-762 (May) 1934. (*d*) Wyllie, J.: A Second Attack of Poliomyelitis After Thirteen Years, Canad. J. Pub. Health **36**: 156-159 (April) 1945.

lar conclusion. Since any plan for the prevention and control of the disease must take into consideration the susceptibility and immunity of the population at large, facts which throw additional light on this question are urgently needed. However, the attack rate of the paralytic form of the disease is so low over a period of twenty or more years that only in large and intense epidemics do opportunities occur for judging clinical immunity. The development of approximately 1,100 cases of poliomyelitis during the summer of 1944 in the area in and around Buffalo, with 6 instances of second attacks, offered such an opportunity.

The study of the development of immunity in poliomyelitis is made particularly difficult by the lack of accepted and reliable criteria for making the diagnosis. As discussed in a previous report,[2] the occurrence of a large number of extremely mild and abortive forms of the disease, which can be recognized only by means of epidemiologic studies and proved only by inoculation of monkeys, makes it difficult to define accurately what constitutes a second attack of the disease. The presence of flaccid paralysis is of course a reliable basis for judgment, but since many workers feel that such cases constitute only 5 to 20 per cent of any total epidemic, studies are needed in regard to the development of immunity in the milder forms as well. In the following report, certain facts are presented which have been derived both from diagnosed cases of the disease and from minor illnesses which on epidemiologic and circumstantial evidence appeared also to have been caused by the virus of poliomyelitis.

PRESENTATION OF CASES

During the summer of 1944, in the area in and around Buffalo, a diagnosis of poliomyelitis was made in the cases of 6 persons who had had the disease previously.

CASE 1.—*First Attack.*—At the age of 9 years this girl was taken sick with headache, fever and stiffness in the back, with later progression to paralysis of the right leg. The acute illness subsided after about five days, but the paralysis was sufficiently serious to require surgical stabilization several years later. Admission to a hospital had occurred at the end of the acute illness, and no lumbar puncture had been done. A brother was also admitted to the hospital with poliomyelitis at the same time, and a second brother had a mild attack at home.

Second Attack.—During the height of the 1944 epidemic, fever, headache and tingling sensations in one leg developed in the patient who was now 27 years of age. On the following day the leg became paralyzed, and she was admitted to the hospital. The spinal fluid obtained by lumbar puncture was found to contain 52 cells per cubic millimeter and to have a protein content of 75 mg. per hundred cubic centimeters. Fever continued for six days. There was some return of function during her thirty-five days in the hospital.

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2. Bridge, E. M.: The Diagnosis of Abortive Poliomyelitis: A Study of Illnesses Occurring in 1123 Contacts of Patients with Poliomyelitis, J. Pediat., to be published.

CASE 2.—*First Attack.*—This patient had her first attack of poliomyelitis at the age of 6 years. Two weeks previously a tonsillectomy had been performed. The illness began with a persistent severe headache, probably fever and weakness of both legs. On the following day there were nausea and stiffness of the neck and back. This persisted until the time of the patient's admission to the hospital. The spinal fluid was found to contain 119 cells per cubic millimeter, and to show a slight increase in protein. Fever continued for three more days in the hospital, and she was discharged after two weeks. Weakness of the left leg persisted for about one and one-half years, but gradually disappeared during the following three years.

Second Attack.—At the height of the 1944 epidemic this girl, now 17 years old, was intimately exposed to a patient with paralytic poliomyelitis during the prodromal stage. About two weeks later headache and malaise developed, and soon there was stiffness of the neck and back. When she was admitted to the hospital, her spinal fluid was found to contain 200 cells per cubic millimeter and there was a slight increase in protein—44 mg. per hundred cubic centimeters. Definite weakness of one leg soon became apparent. This failed to disappear during her month of care in the hospital and is still noticeable two years after the second attack.

CASE 3.—*First Attack.*—During the summer when this child was 3 years old, she was taken sick with fever, vomiting and stiffness of the neck, which were soon followed by paralysis of both legs. The illness lasted about a week, but persistent weakness of both legs remained for four months. In running she was troubled by a loose swinging motion of one foot for several years thereafter. She was cared for at home during this illness.

Second Attack.—During the 1944 epidemic in Buffalo, there were cases of poliomyelitis in the neighborhood where this 15 year old girl lived. Her younger brother was taken sick in the early summer, with the usual symptoms associated with the nonparalytic form of the disease, including stiff neck, but he received no medical aid. Two weeks later the patient began to suffer from fever, vomiting, violent headache, backache and weakness of both legs. Although she was hospitalized and a diagnosis of poliomyelitis was made, the parents refused to permit a lumbar puncture. After several months of physical therapy the weakness of the legs disappeared.

CASE 4.—*First Attack.*—This 8 year old boy was taken sick at the end of the summer of 1941 with headache, vomiting, sore throat, fever and pain in the ankle on walking. Stiffness of the neck and back soon developed leading to his admission to the hospital. The spinal fluid was found to contain 46 cells per cubic millimeter. The fever lasted a week, and convalescence was uneventful. No definite paralysis was present at any time, but the clinical picture appeared typical of poliomyelitis.

Second Attack.—The patient was 11 years old at the time of the epidemic of 1944, when several of his close friends and neighbors had poliomyelitis. He was taken sick with fever, headache and constipation associated with stiffness of the neck and back. Complete paralysis of one arm, with weakness of the other, soon developed. When he was admitted to the hospital, the spinal fluid was found to contain 25 cells per cubic millimeter. After a year paralysis of the arm still persisted.

CASE 5.—*First Attack.*—In September 1940, this 15 year old boy was taken sick with persistent headache and probably with fever.. Nausea and vomiting soon ensued, with pain and stiffness of the neck and back. Because of mild weakness in the legs and arms, he was admitted to the hospital, where a lumbar puncture

showed the spinal fluid to contain 230 cells per cubic millimeter. The weakness gradually disappeared during the month of hospitalization.

Second Attack.—At the height of the 1944 epidemic, a headache with diarrhea developed in this boy, now 19 years old. He also became nauseated and had aches and pains throughout the body. There was extreme tenderness of the extremities but no real paralysis. Both the neck and the back were stiff. The spinal fluid was found to contain only 2 cells per cubic millimeter. The patient had been living in an area where poliomyelitis was prevalent, but no specific contact could be ascertained.[3]

CASE 6.—*First Attack.*—This patient was 2 years old during the summer of 1939, when poliomyelitis was prevalent in Buffalo. An older brother had been ill with fever, vomiting and pain in the neck two weeks before symptoms developed in the patient. The patient herself complained of fever, irritability, stiff neck and an abnormal gait when attempting to walk. She was seen by a health officer working with contagious diseases, who diagnosed her illness as poliomyelitis and had her admitted to the hospital. Here the spinal fluid was found to contain 7 cells per cubic millimeter. A diagnosis of a mild, nonparalytic form of the disease was made.

Second Attack.—In July 1945, when the patient was 7 years old, she again became sick, at the same time that poliomyelitis developed in a brother and in an uncle. At first she complained only of listlessness, but she soon vomited and a stiff neck developed. A speech defect was noted soon afterward. When she was admitted to the hospital, spasm of the hamstring muscles was observed, and the spinal fluid was found to contain 35 cells per cubic millimeter. Weakness of one arm and of both legs was present for a time, but the weakness cleared during the four months of hospitalization.

Of the 6 patients 3 had definite weakness or paralysis with both attacks. Patient 4 showed paralysis during the second attack but had only changes in the spinal fluid to confirm the diagnosis in the first attack. In one of their attacks both patients 5 and 6 had symptoms which cannot be stated positively to have been caused by the virus of poliomyelitis, since no paralysis developed and the spinal fluid was found to be normal. However, both attacks occurred during epidemics of the disease, and the symptoms were consistent with those encountered in the so-called abortive cases. Changes in the spinal fluid do not necessarily occur in mild forms or even in severe forms of the disease.[4] Because of the impossibility of proving the diagnosis, cases 5 and 6 are therefore classed as "probable" instances of second attacks.

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3. It should be noted that approximately 10 per cent of the patients seen during the epidemic of this year had spinal fluid cell counts of 10 or less per cubic millimeter. (Also see Trask and Harper.[4])

4. Trask, J. D., and Harper, P. A.: A Diagnostic Problem in Poliomyelitis: A Consideration of Typical and Suggestive Cases Showing Normal Spinal Fluid, Yale J. Biol. & Med. **5**:155-163 (Dec.) 1932. Wilson, J. L.: Poliomyelitis, in Christian, H. A.: Oxford Medicine, New York, Oxford University Press, 1940, vol. 5, p. 107.

In order to determine whether the occurrence of 4 definite and 2 probable instances of second attacks of poliomyelitis in the Buffalo epidemic offered a basis for judging clinical immunity, calculations were made as described by Earl B. Phelps.[5] During the previous twenty year period, 1,151 cases of the disease which had not been fatal had been reported to the Department of Health. If one assumes that through movements of the population no significant change has occurred in the number of persons living in the community who have had the disease previously, the attack rate among this group is 3.5 definite cases per thousand and 5.2 cases per thousand if the 2 probable instances are included also. During the 1944 epidemic 1,058 cases of the disease were reported among the 387,000 people whose ages were 30 years or less. This gives an attack rate of 2.7 per thousand, or an expected number of second attacks of 3. Actually, as has been mentioned, 4 definite second attacks were observed and 2 other probable ones. The data confirm the findings of Fischer and Stillerman and of Nelson and Green and cast doubt on the existence of protective immunity acquired by an attack of the disease.

MINOR ILLNESSES OF A POLIOMYELITIC NATURE OCCURRING IN PERSONS WHO HAVE HAD THE DISEASE PREVIOUSLY

In view of the increasing recognition of the existence of mild forms of the disease, there exists the possibility of second attacks without characteristic features. Does a mild attack protect against subsequent infection or against paralysis? Does a first attack in severe form afford more protection than the mild and often unrecognized abortive attacks? These are questions to which there are at present no answers in the clinical literature. Yet as a basis for understanding the susceptibility of the population at large to poliomyelitis, answers are needed. Needless to say, studies of these aspects of immunity are inhibited by the impossibility of making a positive and undeniable diagnosis of the mild forms of poliomyelitis without the time-consuming and expensive procedures involved in experiments with monkey inoculation. Until simpler and more readily available laboratory methods are developed, the epidemiologic approach continues to be the only means at hand for drawing conclusions.

As a step toward securing additional information regarding the immunity conferred by a former attack of the disease, 168 persons who had had poliomyelitis one to twenty years previously were studied. Through questionnaires and interviews data were obtained concerning exposure of these persons to known instances of the disease during the epidemic of 1944 and concerning the appearance of symptoms of any kind. From other studies to be reported elsewhere,[6] it was known that during the epi-

5. Phelps, E. B., cited by Fischer and Stillerman.[1a]

6. Bridge, E. M.: To be published.

demic and closely parallel in time relations to the reported cases there had occurred an intense outbreak of minor illnesses similar in most respects to those known to be caused by mild infections with the virus of poliomyelitis. It was of interest to learn whether former patients were relatively free from this type of minor illnesses during the epidemic period and whether or not any former patient had acquired symptoms consistent with a mild second attack of the disease.

A study of the data obtained from these 168 former patients revealed that 77 persons had been living in neighborhoods where poliomyelitis was present and that 20 had been exposed to persons known to have the disease. The remaining 91 knew of no reported cases in the immediate neighborhood and said they had not been exposed. However, no information was available concerning exposure to illnesses other than diagnosed poliomyelitis. The results are recorded in the table. It will be

Incidence of Later Illnesses Regarded as Being Possible Mild Poliomyelitic Infections and of Other Nonspecific Illnesses Among Patients Who Had Had Poliomyelitis.

Illness	Exposure, Definite or Likely		No Exposure Known	
	Number	Per Cent	Number	Per Cent
Possible mild poliomyelitis	13	17	0	0
Nonspecific	15	19	37	41
No illness	49	64	54	59
Totals	77	100	91	100

noted that in 17 per cent of the 77 persons who had been exposed, symptoms developed suggestive of a mild attack of the disease. These were illnesses characterized usually by fever and vomiting, sometimes by sore throat and by meningeal signs, transient weakness or muscular spasm. Among those in whom the likelihood of exposure was less, no illness of this character was reported. Several examples will illustrate the type of information obtained.

CASE 7.—This boy of 3½ years was admitted to the hospital during the epidemic of 1939 because of fever, headache and sore throat. Stiffness of the neck, spasm of the hamstring muscles and a spinal fluid count of 11 cells per cubic millimeter were found, and the diagnosis of nonparalytic poliomyelitis was made.

At the age of 8 years, during the 1944 epidemic, the patient played in close contact with a boy in whom poliomyelitis developed during the first week in August. On August 18 the patient became ill with sore throat, painful extremities and probably fever, a condition which lasted four days and left him with a persistent weakness of one leg.

CASE 8.—This child was 8 years of age at the time of the epidemic of 1939, when fever, headache and paralysis of the left leg developed. The diagnosis was made after the subsidence of the acute symptoms because of the weakness which persisted for over a month.

During the 1944 epidemic he attended a summer camp where there were several cases of poliomyelitis. Others were reported in the neighborhood of his home. Ten days after returning from camp he had fever with vomiting and malaise which persisted for eight days, but he had no other characteristic features.

CASE 9.—At the age of 10 years this child became sick with fever, vomiting, headache, stiff neck, weakness of both hands and spasm of the hamstring muscles. He was admitted to the hospital, where the diagnosis of poliomyelitis was made. At the end of two weeks the muscular weakness had disappeared.

A year later, during the 1944 epidemic, he played on August 7 with a boy who died of poliomyelitis five days later. On August 23, exactly two weeks after the exposure, a "cold," with fever, sore throat and generalized muscular pains which lasted for eight days developed. No weakness or paralysis was noted.

In addition to the 3 patients whose cases are described, 10 others had symptoms of a similar nature which led to a diagnosis of probable mild poliomyelitis. All 13 were among the group who were aware of definite exposure to the disease itself. No person among the group in which exposure was absent or uncertain suffered from an illness which gave rise to the suspicion of its being mild poliomyelitis. However, as shown in the table, persons in both groups had minor illnesses of an apparently nonspecific character. While some of these probably represented extremely mild infections with the virus of poliomyelitis, available methods did not permit an accurate diagnosis to be made. While it is, of course, impossible to draw conclusions concerning immunity in poliomyelitis from observations such as these, they serve, nevertheless, as a warning against the sweeping statements which are often made. They also emphasize the limitations of any study of clinical immunity in poliomyelitis which confines attention to the recognized paralytic forms of the disease. Until more adequate means become generally available for the diagnosis of mild forms of the disease, the possibility of second attacks occurring in unsuspected form must be anticipated.

COMMENT

As a result of the observations made by Fischer and Stillerman and by Nelson and Green and of the present study, the incidence of second attacks of poliomyelitis appears to be such as to cast doubt on the existence of any significant clinical immunity following a single attack of the disease. Furthermore, the occurrence of illnesses consistent with mild "abortive" poliomyelitis in persons who have had the disease previously adds emphasis to the necessity of a revaluation of the entire question of immunity and acquired resistance. It has been pointed out by others that the interval between first and second authentic attacks varies from two to twenty-five years, and in case 9, reported previously, the interval is only one year. This variation suggests that second attacks depend on chance exposure rather than on acquired immunity of any particular duration.

The inadequacy of or lack of immunity which follows an attack of the disease is confirmed by numerous observations on laboratory animals. As early as 1913, Kling and Levaditi [7] reported that second attacks could be induced in monkeys. More recent observations [8] have attempted to ascertain the importance of the dosage, the severity of the initial infection and the method of inoculation in the development of acquired resistance, but all agree that if immunity is developed at all it is of uncertain degree and probably of short duration. While more experimental work is clearly needed before conclusions can be drawn, the evidences from both clinic and laboratory suggest that in considering measures to prevent or control epidemics, acquired immunity to the disease cannot be relied on.

If, then, sound evidence for acquired clinical immunity is lacking, some other explanation must be sought for the cyclic occurrence of epidemics and the relative infrequency with which adults acquire the disease as compared with children. Both of these epidemiologic phenomena have been attributed in the past to an increasing degree of acquired resistance as more and more opportunities arise for acquiring infection with the virus in mild and usually unrecognizable forms. Only as the number of young susceptible persons increased was fuel for an epidemic considered to be present. If clinical immunity is slight or negligible, other factors related to the aging process must be sought to explain the low incidence, particularly of the paralytic forms of the disease, among the adult population. Similarly, the epidemic cycle may depend more on the injection of virulent virus into a community in which human movements and contacts are numerous than on the presence of a fresh generation of susceptible persons. The present observations only free the physician from certain misconceptions of the past; future work can do much to make clearer the reasons for the peculiarities of epidemics.

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7. Kling, C., and Levaditi, C.: Études sur la poliomyélite aigue epidémique, Ann.Inst.Pasteur **27**: 718 and 839, 1913; Compt. rend. Soc. de biol. **74**: 316, 1913.

8. (*a*) Burnet, F. M., and Macnamara, J.: Immunological Differences Between Strains of Poliomyelitis Virus, Brit. J. Exper. Path. **12**: 57-61 (April) 1931. (*b*) Flexner, S.: Reinfection (Second Attack) in Experimental Poliomyelitis, J. Exper. Med. **65**: 497-513 (April) 1937. (*c*) Toomey, J. A.: Second Attacks of Experimental Poliomyelitis in Macacus Rhesus Monkeys: Immunity or Lack of Immunity of Homologous and Heterologous Strains of Virus, J. Immunol. **35**:1-12 (July) 1938. (*d*) Kessel, J. F., and Stimpert, F. D.: Immunity in Monkeys Recovered from Paralytic Attacks of Poliomyelitis, J. Immunol. **40**: 61-72 (Jan.) 1941. (*e*) Howe, H. A., and Bodian, D.: Second Attacks of Poliomyelitis: An Experimental Study, J. Exper. Med. **74**:145-166 (Aug.) 1941. (*f*) Faber, H. K.; Silverberg, R. J., and Dong, L.: Poliomyelitis in Cynomolgus Monkey: Resistance to Spread of Infection in Central Nervous System Following Exposures of Mucous Membranes to Virus, with Comments on Non-paralytic Poliomyelitis, ibid. **78**: 519-526 (Dec.) 1943. (*g*) Bodian, D., and Howe, H. A.: Non-Paralytic Poliomyelitis in Chimpanzee, ibid. **81**: 255-274 (March) 1945.

SUMMARY

Four cases are reported of persons having second attacks of poliomyelitis and 2 cases of persons probably having second attacks.

The proportion of these cases to the total epidemic of 1944 in the area around Buffalo is such as to cast doubt on the existence of significant acquired immunity.

When reexposed to the disease some persons who have had poliomyelitis previously may have minor illnesses consistent with a diagnosis of abortive poliomyelitis.

From the literature it is also evident that one attack of poliomyelitis in experimental animals does not confer immunity against subsequent infection.

In the management of cases of the disease as well as of epidemics, it appears inadvisable to rely on acquired immunity to protect persons who may be in close contact with patients.

FAMILIAL GLYCOGEN DISEASE

Report of Four Fatal Cases of the Hepatic Form of the Disease in Siblings of One Family

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IN 1928, van Creveld [1] described a peculiar disturbance of carbohydrate metabolism in a boy who showed enlargement of the liver shortly after birth. Van Creveld expressed the opinion that he was probably dealing with a condition of excess storage of glycogen in the liver, perhaps also in the skeletal muscles, and that this glycogen could be mobilized only with considerable difficulty. Von Gierke,[2] in 1929, then described cases of hypertrophy of the liver and kidneys caused by excess accumulations of glycogen. The storage was not demonstrated clinically, but was found at postmortem examination. The name "glycogen storage disease" was given to the condition. Chemical studies in these cases of von Gierke were carried out by Schönheimer.[3] Since the initial descriptions, many studies on the disorder have appeared in the literature, among which may be cited those by van Creveld,[4] Mason and Andersen [5] and Bridge and Holt.[6]

Briefly, von Gierke's glycogen storage disease is due to abnormal metabolism of glycogen resulting from a congenital defect in that portion of the enzyme system of the liver which converts glycogen to dextrose and dextrose to glycogen.[5] Large accumulations take place in one or more organs, notably the liver and the kidneys, occasionally the heart and the skeletal muscles, with considerable hypertrophy of these organs.

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1. van Creveld, S.: Peculiar Disturbance of Carbohydrate Metabolism in Childhood, Nederl. maandschr. v. geneesk. **15**:349-359, 1928.

2. von Gierke, E.: Hepato-nephromegalia glykogenica, Beitz. z. path. Anat. u. z. allg. Path. **82**:497-513 (Sept.) 1929.

3. Schönheimer, R.: Ueber eine eigenartige Störung des Kohlehydrat-Stoffwechsels, Ztschr. f. physiol. Chem. **182**:148-150, 1929.

4. van Creveld, S.: Glycogen Disease, Medicine **18**:1-128 (Feb.) 1939.

5. Mason, H. H., and Andersen, D. H.: Glycogen Disease, Am. J. Dis. Child. **61**:795-825 (April) 1941.

6. Bridge, E. M., and Holt, L. E.: Glycogen Storage Disease: Observations on the Pathologic Physiology of Two Cases of the Hepatic Form of the Disease, J. Pediat. **27**:299-315 (Oct.) 1945.

There is difficulty in mobilizing this glycogen, which is exceedingly stable even after death and even though death may have resulted from acute febrile disease.[4] The condition differs from other storage diseases in that the glycogen is deposited principally in the parenchymal cells, especially those ordinarily containing glycogen, rather than in the cells of the reticuloendothelial system.[7]

According to van Creveld,[4] glycogen disease manifests itself at or soon after birth and may be compared to a persistence of the fetal state. Shortly after birth some storage of glycogen occurs in various embryonic tissues. This fetal glycogen likewise shows great stability and is not readily subject to mobilization either in the cold or by the use of epinephrine as in the postnatal state. Glycogen may also be found in normal newborn infants in tissues in which accumulations later in life occur only pathologically. These stores are never so great, however, that hypertrophy simlar to that in glycogen disease results.

The disorder may occur as an isolated instance in a family or may affect 2 or more siblings.[4] For example, Schall [8] and Unshelm [9] detailed its occurrence in 2 brothers. Exchaquet [10] described 3 cases of congenital hypertrophy of the liver and retardation of growth in one family, a brother and twin sister. Ellis and Payne [11] reported 3 cases in a family, a brother 19 years of age and two sisters 11 and 14 years. They also described 2 cases in sisters 12 and 15 years of age. The mother of these children was found at necropsy to have an enlarged liver. Ellis and Payne expressed the opinion that the familial tendency in glycogen disease may indicate its inheritance as a mendelian recessive character. No established case of direct transmission from affected parents has, however, been reported.

Moreover, precise information is lacking on the relationship of glycogen disease to consanguinity of parents. In 1 of van Creveld's cases [4] the parents were first cousins. Two of the patients discussed by Unshelm [9] were offspring of a marriage between second cousins. Ellis and Payne [11] expressed the opinion that although the total number of cases is too small to warrant conclusions, the incidence of marriages between first and second cousins in cases of glycogen disease is of possi-

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7. Kato, K.: Glycogen Diseases, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1945, vol. 3, chap. 24, pp. 1-14.

8. Schall, L.: 3 Falle von Glykogenspeicherkrankheit, München. med. Wchnschr. **79**:2078-2080 (Dec. 23) 1932.

9. Unshelm, E.: Die Glykogenkrankheit, Jahrb. f. Kinderh. **137**:257-302, 1932.

10. Exchaquet, L.: Infantilisme hepatique familial, Arch. de méd. d. inf. **34**: 656-667 (Nov.) 1931.

11. Ellis, R. W. B., and Payne, W. P.: Glycogen Disease, Quart. J. Med. **29**:31-49 (Jan.) 1936.

ble significance and further suggests that the condition is inherited as a mendelian recessive trait.

With respect to clinical and pathologic manifestations in cases of glycogen disease, Mason and Andersen [5] have emphasized the wide variations found. These differences are such that reasonable doubt exists that the cases all belong to the form described by von Gierke. Bridge and Holt [6] stated that the clinical diagnosis of glycogen storage disease cannot always be made with precision, since the criteria necessary to establish a diagnosis are not clearly defined. The opinion was also advanced that the variations in symptoms and observations reported lead to the conjecture whether more than one disease entity has been included under the name of glycogen disease.

Aside from pathologic changes observed, among the various signs and symptoms described in glycogen disease the following have been stressed as essential in arriving at a diagnosis clinically: a history of increasing size of the abdomen since birth, difficulty in feeding, hepatomegaly and retardation in growth and development, especially in height.[12] In addition, there are an abnormal sugar tolerance curve after ingestion of glucose and unaccompanied by glycosuria, characteristic sensitivity to injections of insulin, absence of hpyerglycemic response to injections of epinephrine, hyploglycemia and ketosis in the fasting state not accompanied by the usual signs of hypoglycemia and relieved little, if any, by the administration of carbohydrates, a urine of high specific gravity with increased diastase content and acetone bodies, hypercholesteremia, increased blood glycogen and fats and decreased serum diastase.

In order further to illustrate the familial nature of glycogen disease and to emphasize the variations in clinical signs and symptoms, we wish to report the unusual occurrence of 4 fatal cases of the hepatic form of the disease in siblings of a Jewish family. It is of interest in this connection that according to van Creveld [4] in only 1 instance thus far reported was the patient of Jewish parentage, and that only the father of a second patient was Jewish. Of added interest are the early age at which the disorder appeared in each of the siblings and the rapidity with which death ensued after the onset of acute symptoms. As will be seen, 3 infants (cases 1, 2 and 4) died in twenty to forty-eight hours after admission to the hospital, while the fourth infant (case 3) died on the fourth postnatal day.

FAMILY HISTORY

The father, 45 years old, Jewish, was born in this country. In June 1938 he was observed in one of the state hospitals, where the diagnosis was made of paranoia and psychopathic personality. The

12. van Creveld.[4] Mason and Andersen.[5] Bridge and Holt.[6] Kato.[7]

mother, 39 years of age, Jewish, was also born in this country and has a congenital deformity of the hip, a facial paralysis and a speech defect. In 1942, the mother suffered accidental loss of vision of the right eye. Partial loss of vision from cataract of the left eye is also present. Recent psychiatric tests disclosed no unusual personality difficulties. A Wassermann test of the blood elicited a negative reaction. No history of consanguinity of parents could be demonstrated. In all there have been 7 pregnancies, 6 having been carried to full term. The fourth pregnancy terminated spontaneously at about the fourth month of gestation. Only 2 siblings are alive today. K. B., aged 12 years, a boy, the first born, is well, and physical examination disclosed no abnormalities. A roentgenogram of the abdomen showed no enlargement of the liver. The other child, F. B., aged 2½ years, a girl, the fifth born, is also in apparent good health. No physical examination could be made of this child, but according to her private physician the child is doing well and presents no evidence of enlargement of the liver. The second, third, fourth and sixth born children all died during early infancy from glycogen disease.

REPORTS OF CASES

CASE 1.—Sibling L. B., a girl, second in position in the family, was born at full term at the Jewish Maternity Hospital on Sept. 15, 1934. Her weight at birth was 2,950 Gm. (6 pounds 8 ounces). Since birth the baby presented a feeding problem, vomiting after each feeding. The stools were never well formed or of good color. Abdominal distention was always present. Progress was fair until the day before admission to the Beth Israel Hospital, when the infant was 3 months old; at this time vomiting and abdominal distention increased and all feedings were refused. On admission to the hospital, on December 17, the temperature was 102 F. and the rate of respirations was 42. The weight was 3,710 Gm. (8 pounds 3 ounces). There was dyspnea and some cyanosis. The abdomen was tremendously distended, but the liver could be palpated well below the umbilicus and out toward the right iliac crest. There was a moderate nasal discharge, and some reddening of the throat was evident. The lungs appeared clear, and a roentgenogram showed no infiltrations. A blood count showed 19,800 white cells of which 57 per cent were segmented forms and 2 per cent nonsegmented forms. There were 34 per cent lymphocytes. No further laboratory examinations could be made. A specimen of urine could not be obtained. The temperature rose rapidly to 104.6 F., and death occurred twenty hours after admission, on December 18.

Postmortem Examination (Dr. Alfred Plaut).—Gross Pathology: The body was that of a white infant girl 52 cm. long. The abdomen was tremendously distended, and on incision the right lobe of the liver was seen extending down to the crest of the ilium. The stomach and intestines were considerably distended. The liver was large, measuring 15.5 by 10 by 4 cm. Its weight was 409 Gm. The outer surface was smooth and pale purplish brown. On cut surface the acinar structure was distinct with small irregular grayish areas throughout. The heart, lungs, kidneys, thymus, thyroid, adrenals, spleen, pancreas and lymphatic apparatus showed nothing unusual grossly. The pelvic organs were also normal, but the left broad ligament showed a firm gray nodule.

Microscopic Changes: Liver. The structure of the liver was indistinct because of the large size of the cells and the consequent pressure of the trabeculae against one another. The capillaries and the Kupffer cells were not well seen. At points, small accumulations of leukocytes indicated the site of a capillary or small vein which was completely compressed by surrounding epithelial cells. The hepatic cells were so large that in many the nuclei were not on the level of the section. In addition to the large polyhedral cells, there were others irregularly or regularly ovoid, some having nuclei at the periphery. In the hematoxylin-eosin stain, most of the cells appeared empty or contained only indefinite partly diffuse, partly lumpy masses. In the Best stain, the tissue of almost the whole liver appeared filled with fine and coarsely granular red material (glycogen). Some veins were almost entirely filled with material characteristic of glycogen. The bile ducts were normal. Only a small number of hepatic cells gave a positive sudan stain.

Kidneys. The epithelial cells of the convoluted tubules were distended by glycogen as described in the hepatic cells. Some of the cells were of normal size and did not appear clear in the hematoxylin-eosin stain. They were seen filled with glycogen, however, in the Best stain. The glomeruli contained only fine droplets of glycogen with an insignificant amount in the pyramids.

The heart, lungs, adrenal glands, thymus, thyroid, spleen, alimentary tract, brain and hypophysis were essentially normal. Sections of muscle and of cartilage from the larynx were normal. Cultures from material taken from both middle ears showed a growth of Bacillus coli.

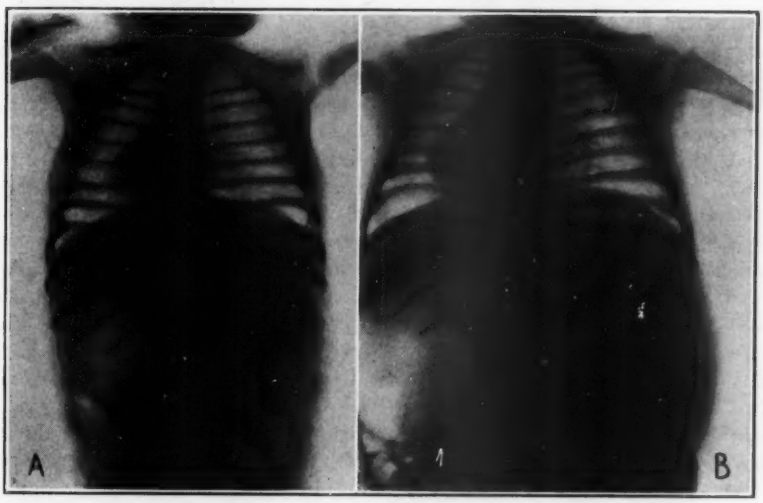
The anatomic diagnosis was: glycogen storage disease (hepatonephromegalic type of von Gierke); dilatation of the stomach and intestines; bilateral otitis media; Marchand's adrenals in the broad ligament.

Summary.—This case was one of glycogen storage disease in an infant girl with a history of difficulty in feeding and of abdominal distention since birth. Signs of acute illness occurred when the infant was 3 months of age and consisted of vomiting, increase in size of the abdomen, fever, respiratory distress and enlargement of the liver. The baby died twenty hours after admission to the hospital for illness. Postmortem examination disclosed glycogen storage disease of the von Gierke type.

Our next experience with the family came ten years later, when another sibling was admitted to the hospital for treatment of an apparently mild illness. This picture changed quickly to one of severe acute illness with death occurring in two days.

Case 2.—Sibling A. B., a girl, the sixth in position in the family, was born by uncomplicated delivery on Nov. 24, 1944, at the Jewish Maternity Hospital. The baby was full term and weighed 3,030 Gm. (6 pounds 11 ounces). On the second postnatal day, labored breathing occurred but nothing unusual was found on examination. No note was made as to the size of the liver. A roentgenogram of the chest showed clear lung fields and a heart of normal contours. Although the roentgenogram included the abdomen no report was made of the presence of an enlarged liver (*A* of the figure). Mild icterus which developed on the third postnatal day cleared quickly. Nothing of further significance took place, and the baby was discharged on the tenth day weighing 2,930 Gm. (6 pounds 4 ounces).

The baby appeared to do well until one day prior to her admission to the Beth Israel Hospital on April 2, 1945, at the age of 4 months. The complaints were of vomiting and watery diarrhea. Physical examination showed a well nourished infant who had a vigorous cry and did not seem very ill. The temperature was 98.8 F. Respirations were labored, however, and the abdomen was so distended as to make difficult accurate palpation of the liver and the spleen. The lungs appeared clear. The results of a single examination of the urine were normal; no acetonuria was present. A blood count showed 3,500,000 red cells with a hemoglobin value of 61 per cent (9.5 Gm.). There were 10,800 white blood cells, of which 29 per cent were neutrophils and 70 per cent were lymphocytes. Wassermann, Kline and Kahn reactions of the blood were negative. A stool culture showed no enteric pathogens. A roentgenogram of the chest revealed



A, roentgenogram of abdomen showing enlargement of liver in sibling A. B. at birth. *B*, roentgenogram of the abdomen showing persistence of enlarged liver in sibling A. B. at 4 months of age.

clear lung fields, but this time a greatly enlarged liver was quickly noted (*B* of the figure). The occurrence of glycogen disease in sibling L. B. (case 1) was immediately recalled, and steps were taken to determine whether we were dealing with a similar condition in this sister.

Blood chemistry studies showed the following: glucose, 30.3 mg. per hundred cubic centimeters; nonprotein nitrogen, 93 mg. per hundred cubic centimeters; cholesterol 172 mg. per hundred cubic centimeters; cholesterol esters, 82 mg. per hundred cubic centimeters; chlorides, 630 mg. per hundred cubic centimeters, and total lipins, 2.66 Gm. per hundred cubic centimeters. Unfortunately no additional studies could be carried out, since the further clinical course proceeded with amazing rapidity to the death of the baby on April 4, 1945, forty-eight hours after admission, even though the infant had not appeared so ill at first. The temperature rose continuously from 98.8 F. to 107.8 F. just before death.

Postmortem Examination (Dr. Alfred Plaut).—Gross Pathology: Examination showed an unusually pale infant girl 61 cm. long. When the abdomen was opened the liver was seen to be enlarged 8 cm. below the ensiform process. In

the anterior axillary line it reached into the pelvis, then running to a level of only 3 cm. above the pubic arch. The liver weighed 584 Gm. and measured 17 by 11.5 by 5.5 cm. It was of doughy firmness and of dull, pale pinkish purple color. The markings of the cut surface were indistinct. Grossly the heart, kidneys, thymus, thyroid, adrenal glands, pituitary, spleen, alimentary tract, pelvic organs, brain and tongue showed nothing of significance. The lungs appeared normal except for areas of atelectasis. The skull and bones were normal. The right middle ear contained brownish green tenacious matter under pressure, and the left more glassy greenish matter.

Microscopic Changes: The liver showed massive fatty change with large droplets. The same hepatic cells contained a large amount of glycogen. The fat droplets were in the peripheral portions of the lobules. The hepatic capillaries were compressed and difficult to see. Many Kupffer cells were large and compact. No fat or glycogen was found in the bile ducts. The structure of the liver was hardly recognizable. The kidneys stained with sudan stain showed the epithelial cells of the primary convoluted tubules large and clear with only a moderate number of basal particles and droplets of sudanophile matter. In the smaller epithelial cells of other tubules a more diffuse fatty change was noted. No fat was found in the glomeruli. With glycogen stain, the epithelium of the primary tubules appeared gorged with glycogen. The secondary convoluted tubules and the straight tubules were normal. Occasional straight tubules contained glycogen in the lumens. The glomeruli did not contain glycogen, but occasionally red masses were situated free in the capsular spaces. The heart showed diffuse fatty changes with small droplets. In the bundle of His the droplets were larger and more numerous.

The thyroid, thymus, adrenal glands, pancreas, pituitary gland, pelvic organs, spleen, intestines and a section from a rib were all normal. The lungs showed alternating distended and collapsed alveoli. Cultures from the throat showed Staphylococcus aureus and nonhemolytic streptococci. Cultures from the middle ear, a lymph node and the intestinal contents revealed no pathogenic organisms.

Here again, the anatomic diagnosis was made of glycogen storage disease (hepatonephromegaly of von Gierke). There were also fatty changes in the liver, partial atelectasis of the lungs, otitis media and anemia.

Chemical Analysis of Organs (Dr. Ella Fishberg).—The various organs listed in the table were assayed by Dr. Fishberg for their glycogen and lipid content as follows: The organs were boiled in 30 per cent solution of potassium hydroxide in a steam bath until all solid matter was dissolved. The glycogen was precipitated out by the addition of an equal volume of 95 per cent alcohol. After centrifuging, normal sulfuric acid was added to the precipitate, which was then placed in boiling water for two hours. The solution was brought to about a p_H 6, and a Folin-Wu determination for reducing substance was made. (This determination of glycogen is an abbreviation of Pflüger's original method.[13])

Some idea of the increased glycogen content of these organs may be had by comparison with the percentages given by van Creveld,[4] who assayed the organs of a child with congenital heart disease (patent ventricular septum): heart, left ventricle, 0.055 per cent; heart, right ventricle, 0.07 per cent; liver, 0.103 per cent; kidney, 0.062 per cent; spleen, 0.01 per cent; skeletal muscle, 0.011 per cent; blood during life, 12.75 mg. per hundred cubic centimeters.

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13. Good, C. A.; Kramer, H., and Somogyi, M.: Determination of Glycogen, J. Biol. Chem. **100**:485-491 (April) 1933.

Summary.—This case of glycogen storage disease occurred in an infant girl with a history of respiratory distress with onset on the second postnatal day. A roentgenogram showed a greatly enlarged liver. The infant became acutely ill in the fourth month of life with vomiting, diarrhea and signs of respiratory distress. A second roentgenogram showed the persistence of the enlarged liver. Blood chemistry studies revealed a glucose value of 30.3 mg. per hundred cubic centimeters and a cholesterol value of 172 mg. per hundred cubic centimeters. A single examination of the urine showed no acetonuria. Death occurred forty-eight hours after admission with hyperpyrexia of 107.8 F. Postmortem

Percentages of Glycogen and of Fat in Certain Organs

	Percentages of Glycogen (Dried Weight)	Percentages of Fat (Dried Weight)
Liver	8.1	39.0
Heart muscle	1.8	19.2
Kidneys	4.1	16.0
Skeletal muscle	0.3	4.2
Spleen	0.15	14.6

examination substantiated the clinical diagnosis of glycogen storage disease. Chemical analysis of the various organs of the body revealed considerable glycogen content.

In view of the deaths from glycogen disease in siblings L. B. (case 1) and A. B. (case 2), investigations were then made of the causes underlying death in the other 2 siblings of the family, sibling K. B. (case 3) and sibling O. B. (case 4). It was our impression that they too had probably died from glycogen disease. The records of their cases and the protocols made at autopsy, as obtained from another hospital, are as follows:

CASE 3.—Sibling K. B., a girl, the third in position in the family, was born on Oct. 25, 1935, at the Greenpoint Hospital, with a weight at birth of 4,760 Gm. (10 pounds 8 ounces). On the second postnatal day spasticity of the extremities appeared. Fever then developed, and respirations became labored and rapid. Harsh breath sounds were heard at the base of the right lung. The anterior fontanel was depressed. On the third postnatal day, the infant's cry became weak. Respirations were rapid and shallow with dilatation of the alae nasi. There was slight ptosis of the left eyelid. A lateral nystagmus was present. The ears, nose and throat showed nothing of significance. There was bronchial breathing at the angle of the left scapula, but there were not any rales or impairement of resonance. The abdomen was distended and tympanitic. The spleen was not palpable, but a firm edge of the liver was easily felt below the level of the umbilicus. On the fourth postnatal day, October 29, the baby's condition worsened and death occurred. The clinical diagnosis was made of cerebral hemorrhage, pneumonia and also possibly syphilis, in view of the enlarged liver.

Postmortem Examination (Dr. R. Aronoff).—Gross Pathology: The body was that of a white infant girl 4 days old. The abdomen was moderately distended. The liver was enlarged, pale brown and flabby and weighed 230 Gm. On section the organ had a dull appearance, was friable and showed cloudy

swelling. The lungs were congested, and the lower lobes of both lungs were consolidated. On section the parenchyma of the lungs was dark, and cloudy fluid exuded on pressure. The mucosa of the bronchi was dark red. The heart, kidneys, thymus, adrenals, skull bones, pancreas, spleen, stomach and intestines were grossly normal.

Microscopic Changes: Sections through the liver showed cloudy swelling and fatty infiltration. The kidneys showed characteristic structure with cloudy swelling of the renal parenchyma. The lungs revealed diffuse bronchopneumonia.

Comment.—The anatomic diagnosis was made here of bilateral confluent bronchopneumonia and hyperplasia of the liver with cloudy swelling. However, because of the history of glycogen disease in other children in the family, a request was made at this time for a review of the pathologic slides from this infant. Since ten years had elapsed no fixed material, paraffin blocks or unstained slides were available. Best's carmine stains had not been made. Only a set of hematoxylin-eosin slides was at hand for reexamination. After review, it was the opinion, both of Dr. Plaut and of the pathologist who originally examined the slides, that the morphologic changes in the sections from the liver were highly suggestive of glycogen storage disease and in keeping with that diagnosis, especially in the light of the histories and pathologic findings in the other siblings of the family.

Summary.—This infant girl had a history of respiratory distress on the second day of postnatal life, when an enlarged liver was noted. The baby died on the fourth day, presumably from confluent bronchopneumonia. A review of the pathologic slides, ten years later, showed evidence consistent with the diagnosis of glycogen disease, even though slides stained with Best's carmine and other confirmatory laboratory evidence were not available.

Case 4.—Sibling O. B., a boy, fourth in position in the family, was born on Sept. 30, 1940, at the Beth Moses Hospital; his weight at birth was 3,855 Gm. (8 pounds 8 ounces). Four days after birth the baby experienced "difficulty in breathing and was placed in a steam room for nine days." Recovery is stated to have been uneventful, and the baby was discharged from the hospital on the eleventh postnatal day.

Progress was apparently satisfactory until the morning of the day before admission to the Greenpoint Hospital, December 1, when the age of the baby was 3 months. The infant refused feedings and vomited any milk ingested. Later in the day difficulty in breathing and a hoarse cry developed. There was not any cyanosis or stridor. Examination disclosed a well nourished infant in respiratory distress. The skin, mucous membranes of the mouth and tongue were dry. The abdomen was considerably distended. A sharp edge of the liver was palpated extending from below the right iliac crest up to a little above the umbilicus anl then curving toward the left costal margin. The heart and the lungs were normal. The neurologic examination did not reveal any abnormality. A urinalysis did not show any albumin or sugar, but gave a 4 plus reaction for acetone. A roentgenogram of the chest and the abdomen showed clear lung

fields. The liver was, however, greatly enlarged and displaced the intestines to the left lower quadrant. The cortex of the left femur showed pronounced thickening. During the afternoon of the first hospital day, a small amount of black fluid was seen coming from the baby's mouth. Sufficient quantity could not be collected for laboratory diagnosis. Later in the day a similar fluid stained the baby's lips. A tourniquet test gave a negative result after ten minutes. The bleeding time was five minutes, and coagulation time four minutes. No further laboratory tests were made. The baby died the following morning, December 2.

Postmortem Examination (Dr. R. Aronoff and Dr. L. J. Fox).—Gross Changes: The body was that of a well nourished white boy weighing 5,900 Gm. with a length of 61 cm. In the right midclavicular line the margin of the liver was 11 cm. below the costal border, the tip being in the pelvis. It was 5 cm. below the xiphoid process and 2 cm. below the costal margin in the left midclavicular line. The liver weighed 800 Gm. and measured 18 by 4 by 0.7 cm. The external surface was smooth and glistening and yellow-brown mottled with darker red areas. The cut surfaces were pale yellow and greasy, and the lobular markings were distinct. The external and cut surfaces of the lungs were normal, but the tracheal and bronchial mucosae were reddened and covered with a small amount of yellow frothy fluid. The heart, kidneys, alimentary tract, spleen, pancreas, adrenal glands and pelvic organs did not show any gross pathologic change.

Microscopic Changes: The lobular structure was not well maintained, and the hepatic cell cords were broad and close to one another. The hepatic cells were swollen with vacuolated or foamy cytoplasm with several small vacuoles, or for the most part one large vacuole, replacing the entire cell. Periportal connective tissue was scant and slightly infiltrated with small round and large mononuclear cells. In special stained preparations, the cytoplasm of the hepatic cells gave a characteristic reaction for neutral fat. Only a small amount of glycogen could be noted in sections stained with Best's carmine stain. The kidneys showed glomeruli of good size and evenly distributed. The convoluted tubules were narrow, and the lining epithelium broad, foamy or vacuolated. The nuclei stained well. The epithelium of the collecting tubules was not remarkable. In special stained preparations the epithelium of the convoluted tubules contained droplets of neutral fat, a similar picture being seen in some of the collecting tubules. The heart, spleen, adrenal glands, thymus, pancreas, bone marrow and brain showed nothing unusual. Sections from skeletal muscles were not made.

Comment.—Anatomically the diagnosis in this case was listed as hepatomegaly (chronic hypertrophic steatosis), acute bronchitis and distention of the stomach and intestines. However, here too, because of the history of glycogen disease in other members of the family, a request was made for a review of the pathologic slides available in this case. The question arose whether we were dealing with an example of hypertrophic steatosis of the liver as described by Bjorum[14] or whether a diagnosis of glycogen disease was tenable. It was again the opinion of Dr. Plaut, to whom the slides were submitted for further study, that the morphologic changes in the liver were consistent with the diagnosis of glycogen disease, even though demonstration with Best's carmine stain was not satisfactory.

Summary.—This infant boy gave a history of respiratory infection at birth. Progress was apparently satisfactory until he was 3 months old, when he became ill with vomiting and respiratory distress. An enlarged liver was then noted clinically and by roentgenography and an examination of the urine gave a reaction for acetone of 4 plus. The baby died twenty-four hours after admission to the hospital. A review of the pathologic slides obtained five years later from another hospital also showed changes in the tissue in keeping with the diagnosis of glycogen disease.

SUMMARY

The case histories and the pathologic examinations of 4 siblings of Jewish parentage who died during early infancy from glycogen storage disease of the von Gierke form are described. Evidence could not be elicited of direct transmission of the disease from the parents, nor could consanguinity of parents be demonstrtaed. Of 6 children in the family 4, 3 sisters and 1 brother, were affected, the signs and symptoms in each instance dating from birth. In fact, considerable enlargement of the liver was shown by roentgenography in 2 siblings at birth (cases 2 and 4), further suggesting a congenital origin of the disease. Among the various signs and symptoms shown by the infants, those of abdominal distention, enlargement of the liver and respiratory distress were outstanding.

It is worth noting that contrary to the accepted opinion of a not unfavorable prognosis in glycogen disease,[4] the 4 cases reported here had rapidly fatal outcomes from underlying acute infection. One infant died on the fourth postnatal day (case 3), 2 died at 3 months of age (cases 1 and 4), and 1 died at 4 months of age (case 2). In the latter 3 siblings, death took place in from twenty to forty-eight hours after admission to the hospital. All essential laboratory examinations could therefore not be made to complete the clinical pictures. Holt and McIntosh[15] have called attention to the mode of death in cases of glycogen disease and have expressed the opinion that the infants succumb from the intractable acidosis accompanying the infection.

Postmortem examinations of 2 babies (cases 1 and 2) showed microscopic changes in the tissue characteristic of von Gierke's glycogen storage disease. A review of the pathologic slides obtained from another hospital five and ten years after death of the other 2 babies (cases 3 and 4), revealed changes distinctive of glycogen disease and in keeping with that diagnosis, especially in view of the family history.

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14. Bjorum, P.: The Occurrence of Fatty Livers in Families, Acta paediat. **6**:225-240, 1926.

15. Holt, L. E., and McIntosh, R.: Glycogen Disease, in Holt, L. E.: Diseases of Infancy and Childhood, ed. 11, New York, D. Appleton-Century Company, Inc., 1939, p. 1326.

PNEUMATOCELE DURING THE COURSE OF PNEUMONIA IN CHILDREN

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THE occurrence of a cavity in the lung during the course of pneumonia in children is a frequent roentgenologic finding. The cavity has a sharply defined thin border and, in a large number of cases, an air-fluid level. These cavities are variously called pneumatoceles, emphysematous bullae or benign cavities. The term "pneumatocele" is preferred by us and will be used in this article. Its derivation indicates a gas-filled tumor or sac.

It is important that the pediatrician and general practitioner be aware of the frequent occurrence of pneumatocele in pneumonia, as it may be confused with a pulmonary abscess or with a congenital pulmonary cyst. If the lesion is recognized as a pneumatocele no treatment is needed and an excellent prognosis can be given.

The use of the term "pneumatocele" in this specific connection was introduced by Zarfl [1] in 1933. He presented a case of a 7 month old infant who contracted bronchopneumonia complicated by empyema in the left pleural space. At the end of the convalescent period a pneumatocele was found in the left lung. This pneumatocele persisted without symptoms for five months, and then resolved spontaneously.

The production of a pneumatocele during the course of pneumonia is purely a problem in aeromechanics. Jackson [2] in 1930 gave the first adequate explanation for this phenomenon. The bronchial tree during inspiration is dilated, and in expiration is constricted. When inflammatory mucosal swelling of the bronchus accompanies pneumonia, it may lead to a check valve action in the bronchus. More air enters the lung past the check valve during inspiration than is permitted to pass through the swollen bronchus on expiration. Obstructive emphysema thus develops. The positive pressure phenomenon was actually demon-

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1. Zarfl, M.: Zur Kenntnis der geschwulstförmigen Luftansammlungen (pneumatocelen) im Brustraum, Ztschr. f. Kinderh. **54**:92, 1932.

2. Jackson, C.: Mechanism of Physical Signs in Neoplastic and Other Diseases of the Lung, J. A. M. A. **95**:639 (Aug. 30) 1930.

strated by Lister [3] using manometric measurements in the living subject. This investigator reported the occurrence of a pneumatocele following pneumonia in a 6 month old infant. The pneumatocele persisted for eleven months before spontaneous and complete recovery. During this period the pneumatocele was needled and pressures were read. These readings varied between plus 2 and plus 4 mm. of mercury on inspiration and plus 4 and plus 10 mm. of mercury on expiration.

The pneumatocele is demonstrable roentgenologically. This not only is a clinical fact, but also has been proved by experimental methods. Laurell [4] inflated the tracheas of excised calves lungs. Emphysematous blebs and bullae thus produced cast ring shadows in the roentgenogram. On microscopic section of these specimens, the ring shadows shown roentgenologically were revealed to be belts of compression atelectasis of the alveoli contiguous with the border of the emphysematous air pockets.

The clinical finding of a pulmonary cavity by roentgen examination brings up the following differential diagnosis as outlined by Caffey [5]: (1) acute pulmonary abscess, (2) aputrid pulmonary necrosis due to infarction, (3) tuberculous cavity, (4) loculated pneumothorax, (5) congenital pulmonary cyst and (6) regional obstructive emphysema in the form of a pneumatocele.

A classification of true pulmonary cystic disease is given by Peirce and Dirkse.[6] This outline is presented to show the relative place of pneumatocele in the classification:

I. True congenital pulmonary cyst or cysts

II. A. Chronic interstitial pneumonitis with emphysema (following bronchopneumonia or unresolved lobar pneumonia)

B. Chronic bullous emphysema (associated with asthma)

III. Cystic bronchiectasis (may occur after bronchopneumonia or aspiration pneumonia in children with resulting changes in bronchi)

IV. Pulmonary pneumatocele—occurring in the course of pneumonia

A review of the world's literature reveals three reported series of cases of pneumatocele following pneumonia. Collen and Hatschek [7]

3. Lister, G.: Pulmonary Pneumatocele (Bullous Emphysema), Am. J. Dis. Child **62**:613 (Sept.) 1941.

4. Laurell, H.: Ein Beitrag zur Deutung der sogenannten Ringschatten in den Lungen, Acta radiol. **10**:72, 1929.

5. Caffey, J.: Regional Obstructive Pulmonary Emphysema in Infants and in Children, Am. J. Dis. Child. **60**:586 (Sept.) 1940.

6. Peirce, C. B., and Dirkse, P. R.: Pulmonary Pneumatocele (Localized Alveolar or Lobular Ectasia), Radiology **28**:651 (June) 1937.

7. Collen, M. F., and Hatschek, O.: Acute Benign Cavitation in Pneumonia, Permanente Foundation M. Bull. **1**:30 (Oct.) 1943.

reported 750 consecutive adult patients with pneumonia among whom 9 cases of pneumatocele were found, an incidence of 1.2 per cent. Benjamin and Childe [8] reported 19 cases in children in a six year period in the Children's Memorial Hospital in Montreal. Caffey [5] reported 20 cases in children in an eight year period at Babies' Hospital in New York city.

The finding of a pneumatocele is essentially a roentgenologic diagnosis. As Collen and Hatschek [7] emphasize, the incidence will depend in some degree on the frequency with which roentgenograms are taken during the illness, inasmuch as a pneumatocele may be transitory. In their series of adult patients, as in all the other reports, pneumatoceles appeared in minimal or in extensive pneumonia at any stage of the illness, but most frequently during resolution. Pneumatoceles usually produce no symptoms and regress spontaneously during a period varying from a few days to several months.

Complications of pneumatocele are rare but possible. Cavities occasionally may rupture and produce a spontaneous pneumothorax. Benjamin and Childe [8] report 2 such cases in their series. Caffey [5] reported 1 case in which the pneumatocele became so large as to cause dyspnea, cyanosis and cough. Even in this instance there was complete spontaneous disappearance of the pneumatocele.

Our own experience consists of 7 cases of pneumatocele occurring during the course of 50 cases of pneumonia in children from April 1, 1945, to March 1, 1946, an incidence of 14 per cent. The cases are tabulated, and only 1 is described in detail. The case of T. H., which follows, was 1 of the most severe. Pleural effusion developed on the right side and his pneumonia resolved slowly under therapy. The other cases varied from extremely mild bronchopneumonia to severe lobar pneumonia with involvement of several lobes. The course, duration, symptoms, signs and treatment of these patients with pneumatoceles did not vary from those of similar patients in whom pneumatoceles did not develop.

REPORT OF A CASE

T. H., a white boy aged 22 months, was admitted to the Pediatric Service of the Permanente Foundation Hospital on July 25, 1945. The present illness had begun six days previously, when a fever and cough had developed. Three days before entry the patient had had a temperature of 103 F. His cough had become increasingly worse and he had pulled at his ears. A diagnosis of bilateral otitis media had been made in the outpatient department. The patient had been started on sulfadiazine, but he had continued to do badly at home. The temperature had remained elevated at about 103 F.

The patient's past history and developmental history were not remarkable.

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8. Benjamin, B., and Childe, A. E.: Localized Bullous Emphysema Associated with Pneumonia in Children, J. Pediat. **15**:621 (Nov.) 1939.

Physical examination on admission revealed a well nourished, moderately ill child with rapid grunting respirations. Both ear drums were moderately injected. The other positive signs were limited to the chest. There was dulness at the base of the right lung and decreased breath sounds, but no rales. The rectal temperature on admission was 102.6 F.

The laboratory work on entry revealed a hemoglobin value of 68 per cent, 4,420,000 red blood cells and 30,650 white blood cells, with 69 per cent neutrophils, 25 per cent lymphocytes, 5 per cent monocytes, 1 per cent eosinophils and 14 per cent stab cells. The urinalysis, tuberculin and Kahn tests gave negative results. The throat smear revealed gram-positive cocci in pairs.

The patient was placed on penicillin therapy with 10,000 units intramuscularly injected every three hours.

Fig. 1.—Roentgenogram taken July 25, 1945, showing massive dense consolidation in the upper lobe and also some cloudy infiltration at the base of the right lung. Some fluid is present in the right pleural cavity.

The roentgenogram of the chest on entry revealed dense infiltration of the upper and of the lower lobe of the right lung, with a right pleural effusion. Because the response to penicillin was slow, the patient was also started on sulfadiazine, 1.5 Gm. per day.

On July 30, five days after entry, a check roentgenogram showed two pneumatoceles, one 2 cm. and one 3 cm. in diameter, with air-fluid levels. There were no changes in the symptoms at this time. The temperature was 100.2 F. The physical examination revealed depressed breath sounds over the entire right lung field with some moist rales.

The patient's course in the hospital was unremarkable. He became afebrile on the sixth hospital day. On the twenty-third hospital day, because of the financial burden on the parents, the child was discharged home on sulfadiazine therapy.

The roentgenogram of the chest at this time revealed the two pneumatoceles. There was still fluid in the right pleural cavity and some infiltration in the right lung field.

Three days after discharge, on August 20, the patient was readmitted because his temperature had risen slowly to 100.8 F. by rectum. His appetite was good and he had no cough.

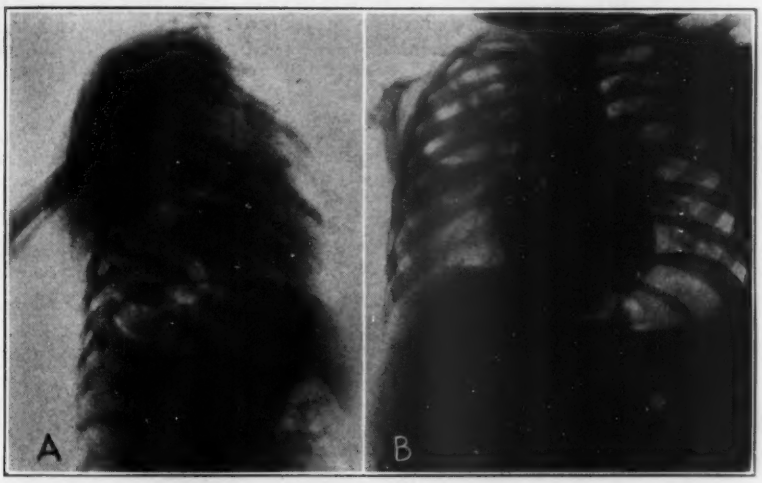

Fig. 2.—Roentgenograms taken July 30. A large cavity with an air-fluid level is present at the base of the upper lobe of the right lung, and a somewhat smaller cavity medial and posterior to it. *A*, lateral view; *B*, posteroanterior view.

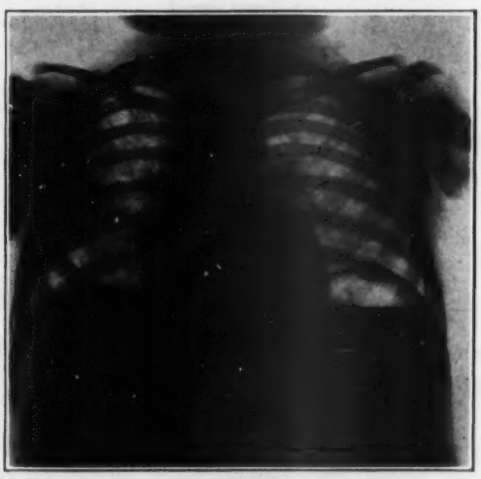

Fig. 3.—Roentgenograms taken October 1. The cavities have disappeared; the infiltration is dissolving.

Physical examination revealed a well nourished, alert, active child who did not appear ill. The only positive findings were dulness at the base of the right lung and decreased breath sounds at the base of the right lung. The blood cell

count showed 5,800 white blood cells, with 30 per cent neutrophils, 61 per cent lymphocytes, 5 per cent monocytes, 4 per cent eosinophils and 3 per cent stab cells. The roentgenogram of the chest was unchanged. The patient was placed on penicillin, 40,000 units intramuscularly injected every four hours. The course was not remarkable. On September 1, the eleventh day after the second admission, the pneumatoceles were no longer seen roentgenologically. Fluid was still present in the right pleural space, and there was a small area of unresolved pneumonia. The patient was discharged on September 4 on a regimen of penicillin, 100,000 units given orally every three hours. Oral administration of penicillin was discontinued after one week.

Cases of Pneumatocele D

Case	Age	Sex	Class of Pneumonia	Anatomic Site	Severity of Pneumonia	Duration of Pneumonia	Time o Appearan Pneumat
J. K.	3 yr.	F	Lobar pneumonia	Upper lobe of left lung	Moderate	19 days	Eighth d of illnes
T. H.	22 mo.	M	Lobar pneumonia	1. Upper lobe of right lung 2. Lower lobe	Severe with right pleural effusion prior to pneumatocele	40 days	Eighth d of illnes
T. W.	11 mo.	M	Broncho-pneumonia	Right middle lung field localization	Mild	8 days	Third da of illnes
K. B.	3 mo.	M	Lobar pneumonia	1. Upper lobe of right lung 2. Middle lobe 3. Lower lobe of left lung, upper lobe	Very severe with right pleural effusion prior to pneumatocele	26 days	Twenty-f day of il
M. T.	11 mo.	M	Lobar pneumonia	1. Upper lobe of right lung 2. Lower lobe	Severe with right pleural effusion prior to pneumatocele	15 days	Eighth d of illnes
C. W.	11 yr.	M	Broncho-pneumonia	1. Middle lobe of right lung 2. Lower lobe 3. Lower lobe of left lung	Mild	10 days	Twenty-f day of il
B. E.	12 yr.	M	Lobar pneumonia	Lower lobe of right lung	Mild	7 days	Second d of illnes

A check roentgenogram taken one month later revealed clear lung fields. The patient has since been completely symptomatic.

COMMENT

Seven cases of pneumatocele developing during the course of pneumonia in childhood have been tabulated. The patients were all boys with one exception. Their ages varied from 3 months to 12 years. Five of the children had lobar pneumonia, and 2 had bronchopneumonia with localization in the middle field of the right lung. The lesion was observed to occur constantly in the area involved by the pneumonia. The pneu-

monia varied from extremely mild to very severe. The pneumonia likewise varied in duration, with a range of from seven to forty days. The time of appearance of the pneumatocele was also variable, ranging from the second day after onset to the twenty-fifth day after onset of the pneumonia. In 1 case the pneumatocele appeared eleven days after the patient had been discharged from the hospital. More than one pneumatocele developed in 3 of the 7 cases. The size of the lesions varied from 1 to 3 cm. in diameter.

ourse of Pneumonia

Site of neumatocele	Number of Pneumatoceles	Size of Pneumatocele	Presence of Fluid Level	Concomitant Symptoms or Signs Due to Pneumatoceles	Duration of Pneumatoceles	Complications of Pneumatoceles	Tuberculin Reaction of Patient	Treatment of Pneumonia
ft lung, upper be	Two	1 cm.	In both	None	2 days	None	Negative	Sulfadiazine and penicillin
ght lung, upper be	Two	3 cm. 2 cm.	In largest cavity	None	31 days	None	Negative	Sulfadiazine and penicillin
ght lung, mid- e lobe	One	1 cm.	No	None	Roentgenogram next day showed cavity larger; actual duration unknown	None	Negative	Penicillin
ght lung, mid- e lobe	One	2.5 cm.	No	None	Patient did not return for follow-up	None	Negative	Sulfadiazine, penicillin, oxygen, blood transfusion
ght lung, upper be	One	1.5 cm.	Yes	None	10 days	None	Negative	Penicillin, sulfadiazine, oxygen, blood transfusion
ght lung, mid- e lobe; lower lobe	Three	1 cm.	In all three	None	7 days	None	Negative	Sulfadiazine, (this patient was admitted and treated for Schonlein's purpura)
ght lung, lower be	One	2 cm.	Yes	None	4 days	None	Negative	Sulfadiazine

Fluid levels were present in 5 of the cases. In none of the cases were there any concomitant symptoms or signs associated with the appearance of the pneumatoceles. In all cases the pneumatoceles were found on routine serial check roentgenograms of the lungs in children with pneumonia. The pneumatoceles observed lasted from four to thirty-one days after their initial discovery. In no case was active treatment undertaken; all disappeared completely and spontaneously.

SUMMARY OF THE PROBLEM

Pneumatocele of the lung occurring during the course of pneumonia is a well demonstrated phenomenon. The incidence of such an occur-

rence is apparently much greater than heretofore appreciated. The demonstration of this fact is dependent on the taking of frequent serial roentgenograms of the lung during the course of the pneumonia because of the ephemeral nature of the lesion involved. The lesion itself apparently results from the accumulation of air behind a check valve produced by inflammatory swelling of the mucosa of the bronchioles during pneumonia.

The differential diagnosis is not difficult. In contrast with the slowly developing and healing necrotic cavity, the pneumatocele may expand and contract rapidly during short periods of time. On roentgenologic examination pneumatoceles may have an air-fluid level. This should not be confused with an acute pulmonary abscess, which is distinguished by foul sputum, fever, clubbed fingers and other signs and symptoms completely lacking in the benign course of the pneumatocele.

The differentiation from tuberculous cavity was dependent in all our cases on a uniformly negative reaction to tuberculin and on the uneventful course. Miller,[9] however, reported a case in which a large emphysematous bulla was mistaken for a cavity in a patient with proved tuberculosis. This was explained at autopsy. The tuberculous inflammatory process had produced a check valve mechanism with a resulting pneumatocele which was not a tuberculous cavity.

Loculated pneumothorax can usually be ruled out by lateral and oblique roentgenograms of the chest. Congenital pulmonary cysts are present on roentgen examination before, during and after the course of pneumonia, whereas pneumatocele is usually not present on the first roentgenograms and disappears during the period of observation.

A pneumatocele rarely produces symptoms or signs. However, the process may become large enough and encroach sufficiently on the vital capacity to produce cough, dyspnea and cyanosis. A pneumatocele may rupture through the pleura, producing a tension pneumothorax.

In the uncomplicated pneumatocele treatment is contraindicated. The aforementioned rare complications may require intervention.

SUMMARY AND CONCLUSIONS

Seven cases of pneumatocele developing during the course of pneumonia in children have been tabulated. This is a common occurrence, the demonstration of which depends on the taking of serial roentgenograms of the chest during the course of the disease. The mechanism consists of the check valve action of bronchiole mucosa involved in the inflammatory process of pneumonia. The differential diagnosis is simplified by the benign, ephemeral character of the lesion. In the uncomplicated case no therapy is indicated.

The roentgenograms were read and interpreted by Otto Hatschek, M.D.

9. Miller, W. S.: A Tuberculous Lung in Which a Large Emphysematous Bulla Was Mistaken for a Cavity, Am. Rev. Tuberc. **28**:359 (Sept.) 1933.

URETHRITIS IN GIRLS

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THE medical profession is to be commended for its awareness of pyelitis and other infections of the upper part of the urinary tract, but, we fear, this has been achieved to the exclusion of an entity which is not quite so frequent but is much more puzzling, even if less serious. Urethritis in girls has received cursory mention but has never been accorded the emphasis which its incidence and importance merit.[1] This entity may be defined as an inflammation of the urethra which is most prominent in the proximal portion and which may extend onto the trigone with or without active demonstrable bacterial infection.[2] Occasionally, it is referred to in passing, although, as a matter of fact, it is not a minor or infrequent annoyance but a major problem little recognized by the general practitioner and pediatrician, and even at times overlooked by the urologist. There are too many patients with the onus of "pyelitis" which never existed at all, because in reality the problem was chronic urethritis improperly evaluated. Though urethritis may be coexistent with pyelitis, it is more often the offending pathologic process when disturbances of urination are present, and there is no more justification for indiscriminately diagnosing "pyelitis" in every child who urinates somewhat frequently, experiences dysuria and has a few pus cells in the urine than there is for calling every rale in the chest a manifestation of pneumonia. It is most important that diagnosis be accurate, for there are few conditions which can be so distressing, yet so simply and gratifyingly treated.

The causation may not be obvious in the individual case, but there are a number of factors for which search should be made. Positive cultures of the urine are found in a minority of cases, but it is probable that bacteria are present in the urethral crypts at some phase of every case. Escherichia coli is the commonest offender when a positive culture is obtained. It is generally conceded that the shortness of the urethra permits easy contamination from the outside and that this

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1. Campbell, M. F.: Pediatric Urology, New York, The Macmillan Company, 1937, vol. 1, p. 503.

2. Folsom, A. I.: The Female Urethra, J. A. M. A. **97**:1345 (Nov. 7) 1931.

accounts for the disproportionately higher incidence in the female. Ordinary uncleanliness and poor personal hygiene may thus be responsible. In some instances vaginal discharge of a nonspecific origin is the source. Masturbation, even by very young children, is rather common, and, we think, a causal factor in a significant number of cases.[3] Conversely, it must be recognized that masturbation may be secondary to urethral irritation and that it may disappear after successful control

Fig. 1.—Cystoscopic view at the vesical neck showing a pronounced granular and inflammatory change particularly evident on the floor of the urethra.

of the urethritis. Acute or subacute recurrences of the chronic form associated with systemic infections, particularly infection of the upper respiratory tract are common and are responsible for many erroneous diagnoses of "pyelitis." Strictures of the urethral meatus are frequently predisposing factors; possibly in many instances the stricture is a part

3. Hinman, F.: The Principle and Practice of Urology, Philadelphia, W. B. Saunders Company, 1936.

of a vicious cycle, the urethritis setting up a periurethral fibrosis and contraction and the resultant stricture aggravating the urethritis.[3]

The inflammatory changes are usually confined to the proximal third of the urethra but may involve its entire length; they frequently extend for a short distance onto the trigone. The acute stage of an attack is evident by a beefy hypervascularity of the entire urethral mucosa, which may, in addition, be thrown into folds. At this stage the region of the vesical neck often assumes a characteristic serrated

Fig. 2.—Cystoscopic view disclosing a villous form of hyperplastic urethritis.

appearance. Usually there is engorgement and edema with heaping up of broad-based mounds of hyperplastic tissue along the urethra, but most prominent in the region of the vesical neck. Such proliferative changes occurring in urethras which are naturally of small caliber loom so relatively large that partially obstructive changes are to be expected and, indeed, are frequently reflected by varied degrees of trabeculation of the bladder. This striking observation has not been sufficiently

emphasized in previous references on the subject. In extreme cases acute urinary retention may occur, as we have seen in 1 patient.

The inflammatory changes may progress to the formation of pedunculated or sessile polypi, or even villous fronds, but this is much less characteristic in children than in adults.[4] Periurethral fibrosis with narrowing of the entire urethral lumen and associated stricture of the urethra are rather common. The persistence of the infection, in our opinion, is probably due to the harboring of bacteria of low virulence

Fig. 3.—Microscopic section (× 100) of hyperplastic tissue in a case of chronic urethritis; invasion by leukocytes and lymphoid cells is prominent.

in the urethral crypts and folds; the bacteria at times are not demonstrable by routine culture.

The clinical manifestations are usually such that one's attention is quickly focused on the lower or the middle portion of the urinary tract. The common triad of symptoms is urgency, frequency and nocturia without accompanying constitutional upset. If any one symptom can

4. McCrae, L. E.: Clinical Cystoscopy, Philadelphia, F. A. Davis Company, 1945.

be called characteristic, it is the sensation of urgency, which is due to the irritative effects of the changes at the vesical neck. This irritation is the underlying factor in a number of patients with nocturnal enuresis whose condition may be relieved by the directing of one's efforts to the urethra. A burning sensation during urination is common. Microscopic hematuria occurs often, and gross bleeding is not unknown. Fever is not a typical finding, but a slight rise in temperature may be present. When considerable pyrexia occurs, it is liable to be a manifestation of accompanying or preexisting systemic disease, such as an infection of the upper respiratory tract. The coincidence of urethritis and acute tonsillitis or otitis media, for example, is rather common. Obstructive urinary symptoms are not often a complaint, but in one of our patients acute retention occurred. General irritability is a common symptom. The urine is usually normal, but varying numbers of pus cells and red blood cells may be found. Cultures may be sterile or may contain the common bacterial offenders found in other parts of the urinary tract.

REPORTS OF ILLUSTRATIVE CASES

Varying clinical pictures seen with chronic urethritis are demonstrated by the following brief résumés of cases:

CASE 1.—*Urgency, Frequency, Nocturia.*—A girl, aged 11 years, was admitted to the Post-Graduate Hospital because of diurnal frequency of urination, nocturia and pronounced urgency. Physical examination revealed no abnormality except for slight vaginal discharge containing numerous gram-positive rods and nonspecific cocci. The urine was normal. Cystoscopy revealed hyperplastic changes at the vesical neck and proximal part of the urethra. Retrograde pyelograms were normal; cultures of urine from both kidneys and the bladder were sterile. The patient's symptoms improved after cystoscopy, and they disappeared after several dilations of the urethra.

Temporary improvement following cystoscopy is not infrequent and at times assumes the proportions of a therapeutic test.

CASE 2.—*Enuresis.*—A girl, aged 6 years, was admitted to the Post-Graduate Hospital because of nocturnal enuresis, diurnal frequency of urination and a burning sensation on urination following acute nasopharyngitis two weeks previously. Physical examination revealed no abnormality. In the urine there was an occasional white blood cell and there were 1 to 4 red blood cells per high power field. Cystoscopy showed considerable congestion and hyperplastic change of the urethra, serration of the mucosa at the vesical neck and pronounced trabeculation of the bladder. Cultures of urine from the kidneys and the bladder were sterile. Pyelograms were normal. Enuresis subsided immediately after cystoscopy and has not returned. Other symptoms immediately diminished, and subsided completely after several dilations of the urethra at two week intervals.

CASE 3.—A girl, aged 7½ years, was admitted to the Post-Graduate Hospital because of mild abdominal pain of undetermined origin and nocturnal enuresis since birth. General examination revealed no abnormality. The urine contained

10 to 15 white blood cells per high power field. Stenosis at the external urethral meatus required dilation before a no. 16F. panendoscope could be introduced. Cystoscopy revealed severe hyperplastic and granular urethral changes and advanced trabeculation. Complete studies of the upper part of the urinary tract disclosed no abnormality. All symptoms diminished after cystoscopy and disappeared completely after two months of dilations of the urethra.

CASE 4.—*Hematuria.*—A girl, aged 7 years, was admitted to the Post-Graduate Hospital because of gross hematuria and dysuria of several days' duration. Physical examination revealed no abnormality. A culture of urine from the bladder was negative. Cystoscopy revealed a small right ureterocele which was subsequently treated by meatotomy, scattered areas of trabeculation and pronouced hypervascularity of the urethra. Retrograde pyelograms were normal. Symptoms subsided with dilations of the urethra and have not recurred.

CASE 5.—*Complete Urinary Retention.*—Complete urinary retention has been seen only once in our experience. A girl, aged 1 year, was admitted to the Post-Graduate Hospital because of urinary frequency and recurring attacks of fever. A complete urologic study revealed only slight narrowing of the urethra and typical hyperplastic urethritis. After her discharge from the hospital the patient was not brought back for follow-up treatment. Three months later frequency of urination was again complained of, and shortly thereafter acute urinary retention developed. Cystoscopy showed advanced congestive and hyperplastic changes at the vesical neck and trabeculation of the bladder. Weekly dilations of the urethra rendered the patient symptom free.

Diagnosis is relatively easy if one will recognize the possibility of the existence of this entity. Unawareness of the high incidence of urethritis, or assumption that the more commonly stressed "pyelitis" or other infection of the upper urinary tract is the cause may lead to incorrect diagnosis. When symptoms referable to the urinary tract coexist with constitutional manifestations, though abnormal elements in the urine are not found, urethritis should be strongly suspected. While chronic urethritis can be presumed in such cases, its presence can be definitely established only by cystoscopy and elimination of the upper part of the urinary tract as the pathologic site. Thus, complete urologic study, including cystoscopy, pyelography and cultural studies of separate specimens of urine from the kidneys and the bladder, is essential, particularly when the urine contains abnormal cellular elements. This should be done with the patient under general anesthesia, for attempts without anesthesia, especially in younger children, cause so much mental and physical trauma to an already irritated child, and to such inconclusive results, that they are better left unmade. The use of the McCarthy panendoscope is of inestimable value, since typical pathologic changes, even when minute, are obvious when seen in profile by foroblique vision, and they often go unrecognized with the right angle vision telescopes. In a less positive way, the therapeutic response to dilation of the urethra is of some diagnostic assistance when the symptom-producing properties of the urethral changes are difficult to estimate.

Treatment is ordinarily rather simple. The overwhelming majority of patients will respond to dilation of the urethra which at the beginning is at weekly intervals for several sessions; subsequently the intervals between treatments may be lengthened. The largest dilating instrument consistent with comfort should be used. Symptoms usually begin to diminish within a few days, and complete relief usually occurs within six to eight weeks. Irrigations and bladder instillations may be used, but are not necessary. Fulguration has not been necessary in our experience. If a good response to treatment has not occurred within six to eight weeks, it is probable that the urethritis is not the basis of the patient's complaints, and that the observations with respect to the urinary tract should be reevaluated. Recurrences are common, particularly with systemic infections, and should be treated promptly.

Foci of infection must be removed. If personal hygiene is at fault, it should be corrected. In persistent cases, masturbation should be suspected, and eliminated if present. When positive cultures of the urine are obtained, appropriate medication should be instituted, varying with the offending organism.

COMMENT

Existence of chronic urethritis in girls is much more prevalent than is generally recognized, and many girls have grown into adulthood with "bladder trouble" because the entity has been overlooked. The simplicity and effectiveness of treatment are such that failure of awareness and diagnosis of the pathologic process becomes an indictment of the physician. The cases cited are illustrative of symptom complexes which may exist in their "full blown" state or to a lesser degree, and it is in the latter group of cases that casual disregard by the physician is to be deplored. It is incumbent on the pediatrician to become as fully aware of the lowermost portion of the urinary tract as he is of the kidneys themselves, and to know that this short tubular structure, the urethra, of the girl can be productive of distressing symptoms.

SUMMARY

Attention is called to a little recognized entity, that of urethritis in girls, productive of a number of urinary symptoms generally attributed to pathologic changes of the upper urinary tract. Illustrative reports of cases are given to show the wide variation in symptoms that may be present, although the same basic pathologic features of chronic inflammatory urethral change characterize all of the cases. Diagnosis is made by direct observation with the cystoscope and elimination of the upper urinary tract as a causative factor. Treatment is simple, consisting of dilation of the urethra; the prompt response is gratifying. A plea is made for awareness and recognition of this ailment.

Case Reports

OSTEOCHONDRODYSTROPHIA DEFORMANS (MORQUIO'S DISEASE)

Observations at Autopsy in One Case

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IN 1941, we reported 3 cases of osteochondrodystrophia deformans [1] (eccentro-osteochondrodysplasia). In 2 of these the disease was far advanced, and in 1 it was thought to represent an early stage. No detailed report of an autopsy on a patient with osteochondrodystrophia deformans exists in the literature. Recently 1 of these 3 patients (case 2, C. P.) died, and observations at autopsy were made available for this report.

Osteochondrodystrophia deformans, or Morquio's disease, is a skeletal disease characterized by (1) dwarfism, (2) deformities of the bones of the trunk and the extremities and (3) changes observed roentgenologically consisting of absence of centers of ossification and destruction, rarefaction and proliferation involving all of the bones of the body, including, directly or indirectly, those of the skull.

In 1929, Morquio [2] described a form of osseous dystrophy occurring in 2 of a family of 5 children, and in 1935 he reported 2 additional cases. In 1931 Ruggles [3] described the roentgen findings in the bones in 8 similar cases, in 5 of which the condition was familial. Another case was added in 1932 by Meyer and Brennemann.[4] During the past

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* The American Philosophical Society held at Philadelphia for Promoting Useful Knowledge gave financial support from the Daland Fund.

1. Einhorn, N. H.; Moore, J. R.; Ostrum, H. W., and Rowntree, L. G.: Osteochondrodystrophia Deformans (Morquio's Disease): Report of Three Cases, Am. J. Dis. Child. **61**:776-794 (April) 1941.

2. Morquio, L.: Sur une forme dystrophie osseuse familiale, Arch. de méd. d. enf. **32**:129-140 (March) 1929; **38**:5-24 (Jan.) 1935.

3. Ruggles, H. E.: Dwarfism Due to Disordered Epiphyseal Development, Am. J. Roentgenol. **25**:91-94 (Jan.) 1931.

4. Meyer, H. F., and Brennemann, J.: A Rare Osseous Dystrophy (Morquio), Am. J. Dis. Child. **43**:123-135 (Jan.) 1932.

thirteen years at least 30 new cases have been recorded in the literature under the name of either Morquio's disease or osteochondrodystrophia deformans.

In 1908 Drysdale and Herringham,[5] in a paper entitled "An Undescribed Form of Dwarfism," reported the cases of 3 sisters who showed deformity and dwarfism. Although the authors presented no roentgenographic evidence, it is possible that their cases belonged to the group described by Morquio. Between 1910 and 1915 several other cases resembling those of Morquio were reported by Bankart,[6] Langmead[7] and Jaroschy.[8] Cases described as instances of familial rickets may likewise have been examples of osteochondrodystrophia deformans, since in many of those recorded in more recent literature at one time or another the condition had been diagnosed as and the patient treated for rickets. It is probable that certain others described prior to 1929 as cases of "atypical achondroplasia," "rachitic chondrodystrophy" and "atypical chondrodystrophy" were instances of osteochondrodystrophia deformans.

There is no group of classic early manifestations which are characteristic of all of the cases of osteochondrodystrophia deformans. Usually the first manifestations of epiphysial irregularity are observed when the child begins to stand or walk. At this time, the parents may note slight kyphosis, enlargement of such joints as the elbows, wrists, knees and ankles or anterior protrusion of the sternum. Some of these changes are thus suggestive of rickets; in fact, it is not surprising to note in how many of the reported cases the first diagnosis was that of rickets. The final picture is essentially that of a dwarf with a normal or slightly enlarged head lodged low between the shoulders on a short stubby neck and resting on a box-shaped torso, an anterior protrusion of the sternum which forms a shelf on which the chin seems to rest, dorsal kyphosis and deformed, more or less useless limbs attached as dangling appendages.

The greatest help in establishing a correct diagnosis is derived from roentgenologic studies. The epiphyses of the long bones are usually irregular, enlarged, flattened and of varying density, suggesting cellular destruction; the heads of the femurs may be absent, misshapen or frag-

5. Drysdale, J. H., and Herringham, W. P.: An Undescribed Form of Dwarfism Associated with a Spatulate Condition of the Hands, Quart. J. Med. **1**: 193-197 (Jan.) 1907-1908.

6. Bankart, A. S. B.: Case of Achondroplasia, Proc. Roy. Soc. Med. (Sect. Stud. Dis. Child.) **6**:155-157, 1912-1913.

7. Langmead, F.: Case of Pseudo-Rachitic Achondroplasia, Proc. Roy. Soc. Med. (Sect. Stud. Dis. Child.) **8**:22, 1914-1915.

8. Jaroschy, W.: Zur Kenntnis des klinischen Bildes der Chondrodystrophia foetalis, Beitr. z. klin. Chir. **83**:379-418, 1913.

mented; the glenoid fossae, or acetabulums, may be irregular, so that articulation with the heads of the articulating bone is improper; the diaphyses are thinned and show areas of uneven density or rarefaction, particularly toward the ends, and the cortex may be thickened on the side of the greatest strain. The small bones of the hands and feet are generally shortened, and examination shows thinning, irregularities of the epiphyses and increased trabeculaton. The centers of ossification of the carpal and tarsal bones are usually deficient in number for the chronologic age. The bodies of the vertebrae are flattened and irregular in outline, with roughened articular surfaces and frequent wedging. Kyphosis in the dorsal and lumbar regions and thickening of the intervertebral disks are usually present. The ribs are widened and flat, and the intercostal spaces are narrowed, with anterior protrusion of the sternum of varying degree.

REPORT OF CASE

A 10 year old Italian boy was admitted to the hospital with the complaints of cough, fever and difficulty in breathing. The parents and a younger sister were living and well. His first cousin had osteochondrodystrophia deformans. There was no other history of similar illness or of consanguinity in the family. The patient was born at term by spontaneous delivery; the birth weight was 4½ pounds (2,041 Gm.). He held his head up at 3 months, began to cut his teeth at 8 months, sat up with support at 12 months and walked at 3 years of age. At 3 months of age he was treated in another hospital for bilateral clubfoot. At 1 year of age the mother observed that protrusion of the chest and curvature of the spine were developing. Aside from frequent infections of the upper part of the respiratory tract, this patient had had none of the usual diseases of childhood. At the age of 4 years he lost control of his sphincters and the use of his legs, and since then he had been completely confined to bed.

Physical Examination.—The child was acutely ill, dyspneic and cyanotic. His temperature was 100 F., his pulse rate 130 and his respiratory rate 40. The systolic and diastolic blood pressures were 100 and 78 mm. of mercury respectively. There was no evidence of mental retardation. The height was 38 inches (97 cm.), the arm span 40 inches (102 cm.), the length from the vertex cranii to the pubis 21 inches (53 cm.), the length from the pubis to the bottom of the heel 17 inches (43 cm.), the circumference of the head 24 inches (61 cm.) and the weight 40 pounds (18 Kg.). The patient was propped up in bed and able to turn from side to side with difficulty, but unable to sit up unsupported. He was obviously a deformed dwarf, with a large oval head flattened laterally and a short neck; the head seemed to rest directly on the shoulders (fig. 1). The bridge of the nose was flat, and the eyes were wide apart. The palpebral fissures were angular and slanting and suggested the facies seen in persons with mongolism. The anteroposterior diameter of the chest was increased; the abdomen was protuberant. There were decided dorsolumbar kyphosis and a definite anterior bulge of the sternum (pectus carinatum), about the size of an orange, on which the chin rested. The upper and lower extremities appeared relatively long as compared with the length of the trunk. Extreme genu valgum and pes planus were noted. The achilles tendons were contracted, producing a bilateral equinus deformity. The ends of the long bones, particularly of the shoulders, elbows, wrists, ankles and knees, were widened.

Neurologic Examination.—The pupils were equal and regular and reacted to light; there was paresis of the right external rectus muscle; the other ocular muscles were unimpaired. The media were clear, and the fundi were normal. There was no nystagmus or weakness of the face, the palate or the tongue. The upper extremities were flaccid; wrist drop was present bilaterally. There was atrophy of the thenar and hypothenar eminences and to a lesser degree of the muscles of the arm, the forearm and the shoulder girdle. The grip was practically nonexistent, there being only a slight amount of power in the upper limbs. There was no fibrillation. The right biceps reflex was hyperactive and the left absent. The muscles of the back were not involved. The abdominal and cremasteric reflexes were hyperactive. There was complete absence of plantar and dorsal flexion of the feet. The boy could elevate his extremities 6 or 8 inches

Fig. 1.—The patient at 7 years of age.

(15 or 20 cm.) above the bed. There was moderate atrophy of the thigh and the gastrocnemius groups of muscles. There was bilateral increase of tonicity, somewhat more noticeable on the left side. Ankle clonus, and Babinski and Chaddock signs were present bilaterally. The knee and ankle jerks were hyperactive; patellar clonus could not be elicited. The sense of pain was unimpaired.

The only other important physical findings were present in the lungs. There was an impairment of resonance over the lower lobe of the left lung; the breath sounds were diminished but no rales were heard.

The hemoglobin was 17 Gm. per hundren cubic centimeters of blood, and there were 5,700,000 erythrocytes and 9,500 leukocytes per cubic millimeter with 72 per cent neutrophils, 24 per cent lymphocytes and 4 per cent monocytes. The urine contained a trace of albumin and an occasional granular cast and red blood cell. Other examinations were not repeated on this admission, but pertinent data have been recorded in a previous report.[1]

Roentgen Examination.—The epiphysial centers of the long bones showed a definite disturbance in growth. The long bones were shorter than normal. There

was actual change in shape of some of the other bones, particularly in the bodies of the vertebrae. At the dorsolumbar junction a number of the vertebral bodies were wedge shaped, with resulting kyphosis. In the cervical region there was demineralization and loss of stature, so that the first cervical vertebra was located at the level of the foramen magnum and farther cephalad than normal. These changes resembled those seen in basilar impression of the skull (platybasia) (fig. 2).

The patient died thirty-six hours after admission to the hospital.

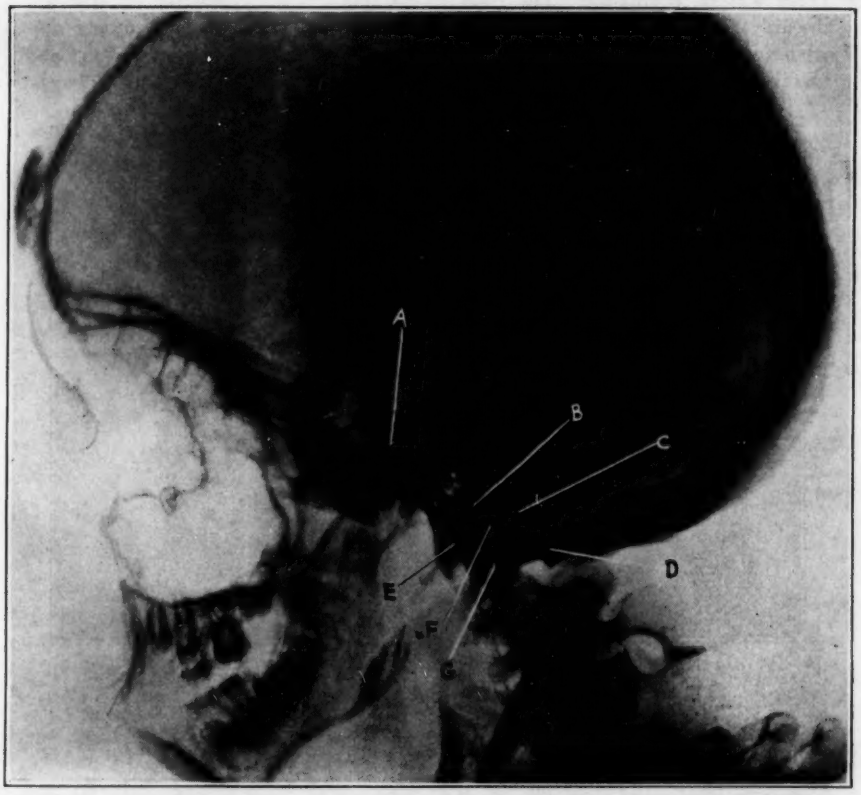

Fig. 2.—A roentgenogram and drawing showing the relationship between the skull, foramen magnum, axis and cervical vertebrae. The clivus is shown at *A;* the anterior and posterior lips of the foramen magnum are indicated by *B* and *C*. The posterior and anterior arches of the first cervical vertebra are shown at *D* and *E*, the odontoid process of the axis appears at *F* and the body of the second cervical vertebra appears at *G*.

Gross Observation at Autopsy.[9]—General: Autopsy performed twelve hours after death revealed a poorly developed boy weighing 40 pounds (18 Kg.) and

9. This autopsy was performed by Dr. E. E. Aegerter, Department of Pathology, Temple University School of Medicine.

Dr. Lawrence Smith, former Professor of Pathology at Temple University School of Medicine, gave us permission to use this material.

measuring 38 inches (97 cm.) in length. The head was enlarged, and the forehead was prominent. The cervical vertebrae showed a posterior curvature, with a compensatory prominence of the anterior thoracic wall so that the head seemed to rest on the anterior thoracic wall. Trunk and extremities were underdeveloped, and multiple deformities of the joints and long bones were observed. The elbow, wrist, knee and ankle joints were irregular and wider than normal. There was some atrophy of the muscles of the shoulders, arms, forearms and hands. A moderate amount of clubbing of both feet was present.

Head and Skull: No abnormalities were observed in the scalp. The bones of the skull were thicker than normal. The dura mater was tense and overlay large amounts of thickened, amber fluid which formed a layer 3 to 7 mm. in depth. The posterior cranial fossa was elevated and was seen almost on the level of the middle cranial fossa. The petrosa on either side was elongated, and the medial portions approximated each other. The atlas, axis, and third, fourth and fifth cervical vertebrae were ankylosed. There was an anteroposterior compression of the cervical spinal canal accompanied with posterior angulation of the cervical vertebrae from the first to the fourth inclusive. The meninges of the cord in this area were thickened and showed numerous fibrous adhesions to the posterior canal wall. The spinal cord was flattened in the anteroposterior diameter to the level of the fourth cervical vertebra.

Brain: The brain weighed 1,335 Gm. and showed no evidence of inflammation or tumor. The third ventricle was dilated, so that there were thinning and protrusion of the floor of the ventricle in the region of the optic chiasm, with some stretching of the chiasm and the optic nerve in this area. The cortex was of normal thickness, and no gross abnormalities were noted in the white matter or the basal ganglions. The pituitary gland was grossly normal in size and appearance.

Thorax: The thorax was underdeveloped. There was an anterior bulge of the sternum measuring about 12 by 12 cm.; the sternum was thickened; the costochondral junctions were enlarged, and the ribs were irregularly flattened and widened. The anterior curvature of the dorsal spine protruded into the right pleural cavity.

Lungs: The pleurae were smooth and glistening. The left and right lungs weighed 75 and 85 Gm. respectively. There was diffuse atelectasis throughout the posterior portions of both lungs, where the bony deformities produced compression of the parenchyma of the lung. There was no evidence of pneumonia, tuberculosis or tumor.

Heart: The heart weighed 120 Gm. There was no apparent shift of the mediastinum. There was no increase in pericardial fluid, and no adhesions were present. The myocardium was firm and showed no gross changes. The anterior surfaces of both ventricles were prominent. No congenital abnormalities were present.

Peritoneum: The lining of the peritoneal cavity was smooth and glistening, and no exudate, excess fluid or adhesions were seen.

Liver: The liver weighed 400 Gm. and protruded below the costal border, possibly as a result of the lateral compression of the chest by the ribs. No gross changes were observed.

Spleen: The spleen weighed 75 Gm.; it was firm in consistency; the capsule was tense, and the cut surfaces were congested.

Pancreas and Adrenal Glands: The pancreas seemed large in proportion to the other viscera. It was firmer than normal. Both adrenal glands appeared normal.

Genitourinary Tract: Each kidney weighed 40 Gm., and examination showed nothing of pathologic significance. Both ureters were moderately dilated, but there was no demonstrable obstruction in the ureters or in the urethra. The wall of the urinary bladder was moderately hypertrophied, the prostate was normal and the testicles were small.

Digestive Tract: The gastrointestinal tract was normal throughout, the appendix was healthy and the mesenteric lymph nodes were not enlarged.

Thyroid: The thyroid gland was grossly normal in appearance.

Vertebrae: A kyphos extending from the ninth dorsal to the second lumbar vertebra was present, and the dorsal and lumbar vertebrae were irregularly flattened except in the area of the kyphos, where considerable wedging was observed.

Microscopic Examinations.—Cervical Portion of Spinal Cord: Compression in the anteroposterior diameter and widening in the lateral diameter were present. The pia mater was thickened. The spinal nerve roots were poorly developed, and extensive glial replacement was noted. Within the substance of the spinal cord there were extensive vacuolation of the fibers, loss of the anterior horn cells and much glial proliferation. There were no foci of inflammation and no tumor. The vessels of the cord showed moderate thickening of their walls but no evidence of degeneration.

Muscle: In the sections of skeletal muscle examined, some atrophy and loss of substance were noted, but there was no fatty or fibrous tissue replacement. The cross striae were distinct, and the sarcoplasm was evenly and deeply stained.

Cartilage and Bone: There were loss and degeneration of the majority of the chondrocytes, with vague foci of vacuolation in the interstitial material of the articular cartilages. There was extensive loss of subchondral bone; the adjacent chondral bone appeared irregular, and the medulla was poorly trabeculated. There was no evidence of tumor, osteoblastic or osteoclastic activity present.

Anatomic Diagnoses.—The anatomic diagnoses were as follows: (1) deformity of the heart caused by compression; (2) massive atelectasis of the lungs; (3) chronic passive congestion of the liver and spleen; (4) congestion of the kidneys, dilatation of the ureters and hypertrophy of the bladder; (5) edema of the brain and possible compression of the spinal cord, and (6) Morquio's disease.

Microscopic Diagnoses.—The microscopic diagnoses were as follows: (1) fatty degeneration and edema of the myocardium; (2) edema of the pleurae and atelectasis of the lungs caused by compression; (3) edema and moderate fatty metamorphosis of the liver; (4) acute congestion of the spleen; (5) compression of the upper cervical region of the spinal cord, and (6) atrophy of voluntary muscle, degeneration of articular cartilage and atrophy of periarticular and subchondral bone.

COMMENT

It is well to attempt to gain some insight into the pathogenesis of the cardinal signs and symptoms of osteochondrodystrophia deformans. Dwarfism may be extreme. The obvious explanation of the tardiness in growth is to be found in the following factors: (1) the underdevelopment and flattening of the bodies of the vertebrae, with resultant shortening of the neck, kyphosis, lordosis and pectus carinatum and (2) the crouching position assumed by the patient together with the genu valgum and the pes planus. The combination of these factors can account for

much of the actual shortening of the body. This explanation, however, may not account for all of the retardation in growth observed. Roentgen studies of the centers of ossification show absences as well as retardation in their appearance; hence there may be an additional factor, possibly endocrinic in nature, which affects development. However, the inclusion of endocrinic dyscrasia as a factor in the causation of the dwarfism is not justifiable with the information available.

The muscular weakness and physical disability in this disease are profound. Chemical analyses of muscle and bone have revealed no noteworthy abnormalities. As the movement of the joints is studied, one is impressed with the restriction present. This sign of epiphysial irregularity is probably one of the earliest clinical indications of the disease. In view of the degree of flabbiness of the muscles and the relaxation of the ligaments, the inference is that this decreased mobility of the joints is due to the extensive changes which occur in their surfaces.

From an orthopedic point of view, Morquio's disease presents a group of interesting deformities, namely: pes planus, genu valgum, coxa vara, scoliosis, kyphosis, pectus carinatum, mild clubhand, humerus varus and skeletal dwarfism. They are due to structural defects in bone and cartilage, to postural changes and to a combination of the two. As stated by Shelling,[10] the structural alterations are covered adequately by the heading osteochondrodystrophia deformans. The postural changes are secondary to the structural and neurologic alterations.

Careful study of these cases makes it obvious that there are two distinct phases of this disease: first, that in which structural defects accompanied with postural changes occur, and, second, that in which neurologic features become manifest. With the appearance of the second phase, the entire course of the disease is altered; the child becomes completely bedridden and eventually helpless. The changes in the bones in themselves do not account entirely for this new picture. One must look elsewhere for a more plausible explanation. For the patient whose case is reported in this paper such a factor, entirely mechanical in nature, was found. This child had a flaccid paralysis of the upper extremities, atrophic musculature and increased tendon reflexes—evidences of pathologic changes in the spinal cord. Roentgen studies revealed a basilar impression of the skull. At autopsy further evidence of the abnormal relation between the first cervical segment and the base of the skull was observed. This abnormality resulted in pressure on the brain stem and upper part of the cervical portion of the spinal cord and pronounced compression of the latter. These observations

10. Shelling, D. H.: Osteochondrodystrophia Deformans, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1945, vol. 4, chap. 29, p. 1.

provide a tenable explanation for the neuromuscular changes observed in osteochondrodystrophia deformans.

SUMMARY

In a fatal case of osteochondrodystrophia deformans a definite abnormal relationship between the first cervical segment and the base of the skull was demonstrated at autopsy. This abnormality resulted in pressure on the brain stem and upper part of the cervical portion of the spinal cord, with the compression of the latter. The neuromuscular changes observed in this patient were secondary to compression of the cord.

PREPYLORIC POLYPUS IN STOMACH OF CHILD DIAGNOSED HISTOLOGICALLY AS ABERRANT PANCREATIC TISSUE

Report of a Case and Review of the Literature

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A BENIGN single polypus is rarely found in the stomach of a child. In the case to be reported the polypus was in a position where it could prolapse through the pylorus into the duodenum and cause obstructive symptoms. In addition, on microscopic examination it was found that this polypus contained aberrant pancreatic tissue.

REPORT OF CASE

In November 1945 a 6 year old white boy was brought to the Mayo Clinic. He had had intermittent umbilical pain for three years and intermittent spells of nausea and vomiting during most of his life.

During the first three months of life this child had symptoms of vomiting after each feeding until atropine was administered, relieving the spasm. At the age of 6 months roentgenologic examination showed a retarded gastric emptying time. From this time, 1940 to 1943, the child experienced only intermittent spells of mild colicky pain around the umbilicus, usually associated with nausea and vomiting.

When he was 4 years of age the intermittent attacks became much worse, occurred from two to three times daily and were associated with an elevation of temperature. This series of spells lasted for two weeks. Roentgenograms were taken, but no definite diagnosis was reached. After this episode the child was relatively free of symptoms for eleven months.

In June 1944, when the child was 5 years of age, he had a recurrence of symptoms with increasing severity. The pain was not associated with the eating of meals or with hunger. There was no regularity to the pain, for it occurred at any time during the day or night. The child discovered that the only way in which he could get relief was to assume a modified genupectoral position; it was not long before he automatically assumed this position whenever the pain began. At the time of this episode a diagnosis of peptic ulcer was made, and the child was placed on a regimen for the treatment of ulcer. However, the spells continued for the next three or four months. In February 1945 this treatment was discontinued except for small doses of antacids when the child had any mild abdominal discomfort. During the summer of 1945 he was completely free of symptoms.

On Oct. 26, 1945 he experienced an acute recurrence of the symptoms. This episode was the most severe, the patient showing signs of intestinal obstruction, that is, intermittent abdominal cramps localized around the umbilicus, accompanied with increasing intensity on the occurrence of each series and ultimately resulting in vomiting. A roentgenologic study revealed a small gastric polypoid mass in the prepyloric region where it would be possible for it to prolapse through the

pylorus into the duodenum. The symptoms lasted four days. From that time until his arrival at the Mayo Clinic, he had recurring mild discomfort, relieved only by assuming the genupectoral position.

The physical examination showed nothing significant except moderate obesity. On surgical consultation the diagnosis of a prepyloric gastric polypus was made with the aid of further roentgenologic studies, and exploratory laparotomy was advised.

At the operation a small polypoid lesion in the prepyloric end of the stomach was found in exactly the same position as seen by the roentgenologist, approximately 1 cm. from the pylorus toward the greater curvature. The mass was 1.5 cm. in diameter (fig. 1). It had a pedicle long enough to convince the surgeon that with a slight invagination of the gastric mucosa this mass could have prolapsed through the pylorus and caused the symptoms described in the history. The polypus was excised, and on microscopic examination was found to contain aberrant pancreatic tissue, both ducts and acini, but no islet cells. It arose from the gastric submucosa (fig. 2).

The child had an uneventful convalescence.

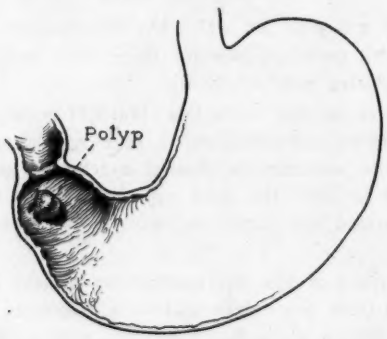

Fig. 1.—Position of the pancreatic rest with polypoid appearance in the prepyloric region of stomach.

GASTRIC POLYPI AMONG CHILDREN

Numerous studies have been made of polypi in the small intestine,[1] the colon,[2] the sigmoid [3] and the rectum [4] of children, but little mention has been made of gastric polypi. In a survey of the literature

1. Atakam, A. M.: Polypose de l'intestin grêle, Presse méd. **2**:2065-2066 (Dec. 19) 1936. Noto Campanella, C.: Poliposi itestinale diffusa in un lattante, Rinasc. med. **17**:299-300 (June 15) 1940.

2. (*a*) Kennedy, R. L. J.; Dixon, C. F., and Weber, H. M.: Polypoid Lesions of Colon of Children, Surg., Gynec. & Obst. **77**:639-644 (Dec.) 1943. (*b*) Kennedy, R. L. J.: Polyps of the Colon and Rectum in Infants and Children, Proc. Staff Meet., Mayo Clin. **15**:108-109 (Feb. 14) 1940.

3. Yaker, D. N.: Polyp of the Sigmoid in a Child, California & West. Med. **41**:184-185 (Sept.) 1934.

4. Smith, N. D.: Rectal Polyps in Infancy, S. Clin. North America **14**: 713-715 (June) 1934. Kennedy.[2b]

reporting prolapsing benign gastric tumors, only 1 case was found in which the patient was a child. In 1925 Mouat [5] reported the presence of a polypoid mass in the stomach of a 12 year old white girl. This polypus was on the posterior wall of the lesser curvature and had prolapsed through the pylorus, distending the duodenum and causing perforation. This child had had a history of recurrent attacks of epigastric pain and vomiting lasting three to four days at a time. She seemed well between attacks.

Weinberg and Raider [6] recently studied the problem of prolapsing pedunculated gastric tumors. They expressed the opinion that such gastric lesions simulate peptic ulcers clinically. If the polypus, because of a

Fig. 2.—Polypoid tissue showing aberrant pancreatic tissue containing both ducts (*d*) and acini (*a*) (× 75).

ball valve action or by actual prolapse through the pylorus, causes obstruction, there occurs intermittent epigastric distress, ranging from mild, vague abdominal discomfort to acute cramplike pains associated with nausea and vomiting. This distress may be relieved either by the taking of food or more often by a change of position of the body. The polypus may bleed, causing gross hemorrhage manifested in the form of hematemesis and melena, or only a secondary anemia may be present. In the

5. Mouat, T. B.: Two Cases of Polypus of the Stomach, Brit. J. Surg. **13**: 165-168 (July) 1925-1926.

6. Weinberg, T. B., and Raider, L.: Pedunculated Tumors of the Stomach Prolapsing Through the Pylorus, Radiology **41**:52-55 (July) 1943.

case reported here all of these symptoms occurred except the gross hemorrhage or anemia.

Weinberg and Raider stressed the following roentgenologic criteria for the diagnosis of a prolapsed gastric polypus: (1) a central filling defect in the duodenum (if the patient is either in the prone or in the right oblique position); (2) delayed gastric emptying time of more than six hours, and (3) a normal-appearing stomach when the tumor has prolapsed into the duodenum. Our patient fulfilled all three of these criteria.

Pendergrass and Andrews [7] in 1935 reported the case of a 10 year old girl who presented clinically and roentgenologically a picture similar to that of the patient I am reporting. The preoperative diagnosis in this case was of a prolapsing gastric lesion. At operation there was found an abnormal mesenteric membrane binding the duodenum and the stomach down at the pylorus and causing the obstruction.

Weinberg and Raider enumerated eight differential diagnoses to be considered with the foregoing clinical and roentgenologic findings. They are (1) congenital venous anomalies in the duodenal region; (2) duodenal ulcer; (3) pyloroduodenal adhesions; (4) prolapsed gastric mucosa; (5) pressure of the pancreas from beneath the duodenum; (6) hypertrophic duodenal mucosa or polyp; (7) hypertrophic pyloric mucosa, and (8) retained food in the duodenum. To this I should like to add "the presence of aberrant pancreatic tissue in the prepyloric region."

ABERRANT PANCREATIC TISSUE

In an extensive review of the 471 cases of aberrant pancreatic tissue reported in the literature,[8] it was noted that 46 (10 per cent) of the patients were children. Schultz [9] in 1727 described the first instance of aberrant pancreatic tissue. The tissue was found incidentally at necropsy in a diverticulum of the ileum of a newborn infant; however, there was no histologic confirmation. In 1870 Neumann [10] reported ectopic pancreatic tissue, also in a diverticulum of the ileum found at necropsy. This was in a 10 month old boy. This was the first occurrence of aberrant pancreatic tissue in a child to be proved histologically. Of the

7. Pendergrass, E. P., and Andrews, J. R.: Prolapsing Lesions of the Gastric Mucosa, Am. J. Roentgenol. **34**:337-350 (Sept.) 1935.

8. Castro Barbosa, J.: Pancreatic Heterotopia: Clinical and Pathological Studies of Surgical Cases, Thesis, Graduate School, University of Minnesota, 1945.

9. Schultz, J., cited by Hunt, V. C., and Bonesteel, H. T. S.: Meckel's Diverticulum Containing Aberrant Pancreas, Arch. Surg. **28**:425-439 (March) 1934.

10. Neumann, E., cited by Hunt, V. C., and Bonesteel, H. T. S.: Meckel's Diverticulum Containing Aberrant Pancreas. Arch. Surg. **28**:425-439 (March) 1934.

authors reporting cases,[11] all reported only single examples in children as a part of their total collection except Opie,[11j] Taylor,[11n] Branch and Gross,[11r] and Troll,[11w] who reported 2, 6, 13 and 3 cases respectively in which the anomaly was noted in children.

From this series of 46 cases [11] I have found that the most common site for aberrant pancreatic tissue in children is in Meckel's diverticulum (in 32 per cent of the cases). Aberrant pancreatic tissue was also found along the whole gastrointestinal tract from the stomach to the

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11. (*a*) Van Gieson, I.: Accessory Pancreas in the Wall of the Duodenum, Simulating a Tumor, Proc. New York Path. Soc., 1888-1889, p. 93. (*b*) Schirmer, A. M., cited by Hunt, V. C., and Bonesteel, H. T. S.: Meckel's Diverticulum Containing Aberrant Pancreas, Arch. Surg. **28**:425-439 (March) 1934. (*c*) Brunner, C., cited by Hunt, V. C., and Bonesteel, H. T. S.: Meckel's Diverticulum Containing Aberrant Pancreas, ibid. **28**:425-439 (March) 1934. (*d*) Nicholls, A. G.: Note on a Case of Accessory Pancreas, Montreal M. J. **29**: 903-907 (Dec.) 1900. (*e*) Wright, J. H.: Aberrant Pancreas in the Region of the Umbilicus, J. Boston Soc. M. Sc. **5**:497-498 (May 21 and June 4) 1901. (*f*) Turner, G. G.: An Example of Accessory Pancreas, Lancet **2**:1566 (Dec. 3) 1904. (*g*) Bize and Grisel, cited by Hunt, V. C., and Bonesteel, H. T. S.: Meckel's Diverticulum Containing Aberrant Pancreas, Arch. Surg. **28**:425-439 (March) 1934. (*h*) Gardiner, J. P.: A Case of Congenital Hour-Glass Stomach with Accessory Pancreas, J. A. M. A. **49**:1598-1600 (Nov. 9) 1907. (*i*) Clogg, H. S.: Acute Intestinal Obstruction, Lancet **1**:639-640 (Feb. 29) 1908. (*j*) Opie, E. L.: Disease of the Pancreas, Philadelphia, J. B. Lippincott Company, 1910. (*k*) Albrecht, H., and Arzt, L., cited by Hunt, V. C., and Bonesteel, H. T. S.: Meckel's Diverticulum Containing Aberrant Pancreas, Arch. Surg. **28**:425-439 (March) 1934. (*l*) Carwardine, T., and Short, A. R.: The Surgical Significance of the Accessory Pancreas, Ann. Surg. **57**:653-657 (May) 1913. (*m*) Hale, K.: A Study of the Accessory Pancreas, with Report of One Causing Congenital Pyloric Stenosis, ibid. **83**:774-781 (June) 1926. (*n*) Taylor, A. L.: The Epithelial Heterotopias of the Alimentary Tract, J. Path. & Bact. **30**:415-449 (April) 1927. (*o*) Cogniaux, P.: Contribution à l'étude des pancréas aberrants, Arch. franco-belges de chir. **31**:307-317 (April) 1928. (*p*) Moore, R. A.: Accessory Pancreases: Report of a Case with a Discussion of Their Pathology and Origin, Am. J. Path. **5**:407-414 (July) 1929. (*q*) Ross, K.: Accessory Pancreas Causing Intussusception, Australian & New Zealand J. Surg. **3**:88-93 (July) 1933. (*r*) Branch, C. D., and Gross, R. E.: Aberrant Pancreatic Tissue in the Gastrointestinal Tract: A Report of Twenty-Four Cases, Arch. Surg. **31**:200-224 (Aug.) 1935. (*s*) Hill, F. C., and Cohen, L.: Meckel's Diverticulum Containing Aberrant Gastric Mucosa and Pancreatic Tissue, Nebraska M. J. **22**:187-188 (May) 1937. (*t*) Weeks, E. A., and Steinke, C. R.: Congenital Atresia of the Bile Ducts, Biliary Cirrhosis and Accessory Pancreas: Case Report, Arch. Pediat. **44**:391-394 (June) 1927. (*u*) Black, W. C., and Packard, G. B.: Surgical Complications Resulting from the Presence of Heterotopic Tissue in Meckel's Diverticulum, Rocky Mountain M. J. **35**:859-863 (Nov.) 1938. (*v*) Saupe, E.: Ueber einen durch ein Nebenpankreas hervorgerufenen Magenpolypen, Med. Klin. **1**: 384-385 (March 24) 1939. (*w*) Troll, M. M.: Aberrant Pancreatic and Gastric Tissue in Intestinal Tract, Arch. Path. **38**:375-380 (Dec.) 1944. (*x*) Castro Barbosa.[8] (*y*) Schultz.[9] (*z*) Neumann.[10]

ileocecal valve. Wright in 1901 reported the case of a child who had aberrant pancreatic tissue in an umbilical fistula entirely isolated from the gastrointestinal tract.

The age distribution is given in the table. Forty per cent of the patients were children in the first year of life; 27 per cent were 1 to 5 years of age; 11 per cent 5 to 10 years, and 22 per cent 10 to 18 years. In 66 per cent of the cases in which the sex was known, the patients were boys.

Aberrant pancreatic tissue was found only incidentally at necropsy in 65 per cent of the cases. Seventeen (37 per cent) of the children underwent abdominal laparotomy because of either mild or severe

Incidence of Aberrant Pancreas [11]

	Cases	Per Cent
Age *		
Less than 1 year	18	40
1 year to 5 years	12	27
5 years to 10 years	5	11
10 years to 18 years	10	22
Sex		
Boys	27	66†
Girls	14	34†
Sex not given	5	..
Location ‡		
Stomach	5	11
Pylorus	2	4
Duodenum	8	17
Jejunum	6	12
Ileum	5	11
Diverticulum of ileum	5	11
Meckel's diverticulum	15	32
Umbilical fistula	1	2
Cases with symptoms	17	37
Cases without symptoms	29	63
Tissue found at necropsy	30	65
Operation performed; patient died	6	13
Operation performed; patient cured	8	18
Operation performed; outcome not stated	2	4

* Age of 1 patient was unknown.
† Percentage of cases in which sex was known.
‡ One patient had 2 aberrant pancreatic rests in different locations.

abdominal distress. Intussusception, acute pancreatitis (involving the aberrant tissue), invagination of the diverticulum and bleeding were some of the complications resulting directly from the presence of the misplaced tissue. In 2 cases the aberrant tissue was found following abdominal injury resulting in the rupture of a viscus near the site of the ectopic tissue.

In only 5 cases has aberrant pancreatic tissue been reported in the stomach of a child. Gardiner [11b] in 1907 was the first to report such a case. At the necropsy of a 3 month old child who died of starvation with the diagnosis of pyloric stenosis, a congenital hourglass stomach was found to be the true cause. Incidentally, on the posterior surface of the gastric wall a region of aberrant pancreatic tissue was found.

In 1910 Opie [11j] described 2 instances of aberrant pancreatic tissue in the stomach; 1 patient was a Negro boy 11 years of age, and the other was a 4 year old white boy. In both cases the tissue was found incidentally at necropsy. In the latter case aberrant pancreatic tissue was also found in the duodenum.

Taylor [11n] in 1927 reported the presence of aberrant pancreatic tissue in the stomach of a 2 year old boy who had died of tuberculous meningitis.

Saupe [11v] in 1939 reported the only case similar to the one I have reported. The lesion was a gastric polypus proved histologically to be accessory pancreatic tissue. This patient was 18 years old at the time of operation, but his symptoms had been present since the age of 12 years. The clinical and roentgenologic findings were similar to those of my case.

SUMMARY

A prepyloric polypus which proved to be aberrant pancreatic tissue was found in the stomach of a child 6 years of age. In 46 cases aberrant pancreatic tissue has been found in children. In only 5 cases has aberrant pancreatic tissue been observed in the stomach of a child, and only 1 case similar to the one presented here has been reported previously.

AURICULAR FLUTTER AND CONGENITAL HEART DISEASE

Report of a Case

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AND
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AURICULAR fibrillation is not extremely uncommon in children,[1] but auricular flutter in childhood has been reported in only a few cases. Most of these flutters have developed after diphtheria [2] and have usually been paroxysmal.[3] Even less commonly the condition has been associated with congenital heart disease and has been present for weeks or even years. We believe our case represents one of the latter group and we have been able to find only a few similar cases in the English literature.

Lewis [4] in 1915 reported the first case of auricular flutter in an infant. The flutter was paroxysmal, and the details of the case were not given.

Included in the series of children with paroxysmal tachycardia reported by Koplik [5] in 1917 was a boy who had auricular flutter. This 10 year old child was observed for more than two years, and during this time he had numerous attacks of tachycardia. These were often associated with auricular flutter, and the duration of one episode was forty-eight hours. Digitalis was given but the paroxysms continued to recur.

Amberg and Willius [6] reported a child 5 years of age who had many attacks of cyanosis and dyspnea for a period of two and one-half years. Congestive heart failure developed in this patient, and she was treated for a short time with digitalis. One month later auricular

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From the Department of Pediatrics, University of Louisville School of Medicine.

1. Schwartz, S. P., and Weiss, M. M.: Auricular Fibrillation in Children, Am. J. Dis. Child. **36**:22-39 (July) 1928.

2. O'Donovan, P.: Auricular Flutter After Diphtheria in a Child, Lancet **1**: 607-609 (March 23) 1929.

3. Willius, F. A., and Amberg, S.: Paroxysmal Tachycardia with Syncope Occurring in a Child, Am. J. Dis. Child. **38**:551-558 (Sept.) 1929.

4. Lewis, T.: Lectures on the Heart, New York, Paul B. Hoeber, 1915, p. 116.

5. Koplik, H.: Paroxysmal Tachycardia in Children, Am. J. M. Sc. **154**: 834-851 (Dec.) 1917.

6. Amberg, S., and Willius, F. A.: Auricular Flutter with Congenital Heart Disease, Am. J. Dis. Child. **32**:99-104 (July) 1926.

flutter was discovered, and digitalis was again given, but this time to the point of auriculoventricular dissociation. The treatment was not successful, and at necropsy a patent foramen ovale, a hypertrophied and dilated right auricle, a dilated tricuspid ring, a hypertrophied right ventricle and a dilated pulmonary artery were found.

In 1926 Poynton and Wyllie [7] reported the case of a 3½ year old child who had had several attacks of cyanosis since the age of 4 months. A paroxysmal irregularity of heart rhythm was present, which the authors believed to be auricular flutter. This child was treated with both quinidine and digitalis, but the attacks continued to recur. As in the case reported by Lewis and Koplik, the flutter was noted for only short periods and should probably be considered as paroxysmal tachycardia.

Two instances of auricular flutter occurring in newborn infants have been described. One [8] was suspected before birth because of the rapid rate and irregularity of the fetal heart. There was no neonatal difficulty, and the irregularity disappeared on the tenth day without treatment. An electrocardiogram showed impure auricular flutter.

Sherman and Schless [9] reported on a 3 month old infant who had had auricular flutter since birth. The patient had several attacks of syncope and cyanosis during this time. The infant was treated with 4 drops of tincture of digitalis four times a day for eight days, and the pulse rate dropped from 220 to 150 per minute. A month later the rate was still 150 per minute, and the electrocardiogram showed a normal rhythm. The irregularity did not reappear.

Auricular flutter in a child 5 years of age was reported in 1939 by Halbertsma and Hartog.[10] Three years previously this child had an acute infection complicated by congestive heart failure. The patient was given large doses of digitalis, and four months later auricular flutter was discovered. This arrhythmia remained present for three years and then disappeared after digitalis and quinidine therapy. It did not reappear after the medication was discontinued. A systolic murmur was noted, and the authors believed that a patent foramen ovale was present.

Attention should be called to a case of auricular flutter reported by Davis,[11] even though the patient was an adult. It is included in this

7. Poynton, F. J., and Wyllie, W. G.: Auricular Flutter in Infancy, Lancet **2**:371-372 (Aug. 21) 1926.

8. Carr, J. G., and McClure, W. B.: Auricular Flutter in a Newly Born Infant, Am. Heart J. **6**:824-829 (Aug.) 1931.

9. Sherman, J., and Schless, R. A.: Auricular Flutter in a Newborn Infant, J. Pediat. **5**:802-810 (Dec.) 1934.

10. Halbertsma, T., and Hartog, H. A. P.: Auricular Flutter in a Young Infant with Recovery on Digitalis Therapy, J. Pediat. **15**:114-120 (July) 1939.

11. Davis, H.: Congenital Isolated Dextrocardia Developing Auricular Flutter, Lancet **1**:1331-1333 (June 11) 1938.

review because the arrhythmia was found to be associated with a congenital cardiac defect. The patient was 41 years old, and the auricular flutter was present during the last four months of life. Digitalis was given, but she did not respond to treatment. The clinical impression of dextrocardia without complete situs inversus was confirmed at necropsy. There was neither a patent foramen ovale nor enlarged auricles, and it was concluded that the flutter might have been incidental to the dextrocardia.

Auricular flutters associated with coarctation of the aorta,[12] congenital rhabdomyoma,[13] and other congenital lesions of the heart have been reported, but these were paroxysmal in nature and are not included in this review.

REPORT OF CASE

R. B., a 2½ year old white boy, was first brought to the pediatric clinic at the Louisville General Hospital on Feb. 16, 1945 because of "heart trouble" present since birth. The mother had noticed no cyanosis or dyspnea, but shortly after the child was born she had found that the heart had an irregular beat. At the age of 6 weeks he had been examined by a physician who passed him for an insurance policy.

The past history of the mother revealed a nine month gestation without complications. No neonatal difficulty was experienced. The mother had no acute infectious or chronic diseases during her pregnancy.

The developmental and the feeding history were noncontributory. The child had been immunized against diphtheria and pertussis. There had been no previous illnesses and no complaints suggestive of rheumatic fever.

The family history was noncontributory with the exception that the 2 month old male sibling was hydrocephalic. Examination showed no evidence of congenital heart disease in this infant. The maternal grandfather has cardiac disease, the exact nature of which is not known.

Physical examination revealed a well developed, well nourished white boy who appeared to be in excellent health. He was extremely active, and at no time during this and subsequent examinations was there cyanosis or respiratory difficulty. No clubbing of the fingers was seen. The tonsils were slightly hypertrophied. The lungs were clear to percussion, but the asthmatic type of rales were heart throughout both pulmonary fields. The heart seemed to be of normal size and shape on percussion, but the rhythm was totally irregular. The cardiac rate was 90 per minute with no pulse deficit. An absolute irregularity was present, which became more noticeable on exercise. A soft, high-pitched systolic murmur was heard best at the apex; transmission of the murmur was not recorded at this time.

An electrocardiogram made on Feb. 16, 1945 (fig. 1) was interpreted as showing a rate of 140 with absolute irregularity and an auricular flutter with a rhythm of 2:1 and 3:1. The report on a roentgenogram of the chest read: "There is moderate transverse enlargement of the heart and slight prominence of both auricles. The great vessels are normal in size and contour. There is considerable cloudiness in the lower portions of the lungs."

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12. Oelker, D. W., and Stern, N. S.: Coarctation of the Aorta with Auricular Flutter, Memphis M. J. **12**:183 (Nov.) 1937.

13. Wegman, M. E., and Egbert, D. S.: Congenital Rhabdomyoma of the Heart Associated with Arrhythmia, J. Pediat. **6**:818-824 (June) 1935.

The patient was examined monthly in the pediatric clinic. The cardiac irregularity remained, but the systolic murmur was not heard five months later (Aug. 18, 1945). At this time he was admitted to the ward because of diarrhea and vomiting of one week's duration. No symptoms except those associated with acute gastroenteritis were present; he was afebrile, according to the mother.

Physical examination showed the height to be 39½ inches (130 cm.), the weight 30¾ pounds (14 Kg.) and the temperature 100.0 F. (rectally). The child appeared slightly dehydrated. No clubbing of the fingers was present. The

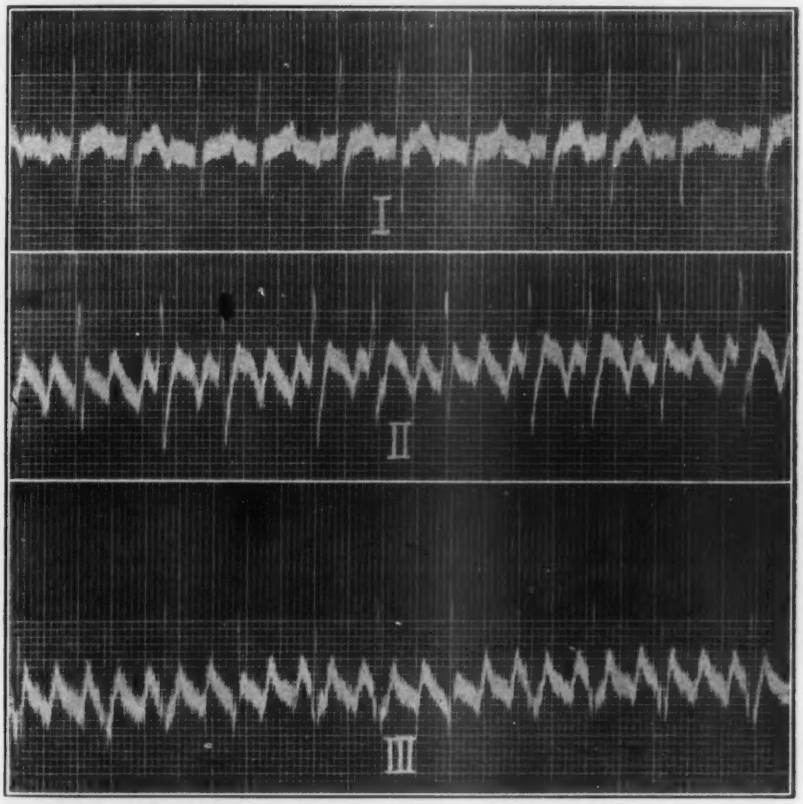

Fig. 1 (Feb. 16, 1945).—First visit of the patient to the clinic. The electrocardiogram (leads I, II and III) shows an auricular flutter varying in type from a 2:1 to a 3:1 block. Ventricular rate 135 to 150 per minute.

pulse was irregular, and the rate varied from 120 to 140 per minute. There was no pulse deficit. No cardiac enlargement was found on percussion. The sounds were of good quality, and except for irregularity no abnormalities were ascertained. The lungs were clear to percussion and auscultation. Abdominal viscera were normal.

With symptomatic treatment the acute gastrointestinal disturbance subsided. Therapy for cardiac arrhythmia was then considered.

Since the electrocardiograms (fig. 2) revealed consistent auricular flutter, the visiting cardiologist was consulted, and therapy with quinidine sulfate was suggested. The pulse rate at this time ranged between 100 and 125 beats per minute. The blood pressure remained around 110 mm. of mercury systolic and 70 mm. of mercury diastolic in the left arm, with corresponding values in all extremities. On Aug. 31, 1945 quinidine sulfate, 0.1 Gm. every three hours, was given orally, and within

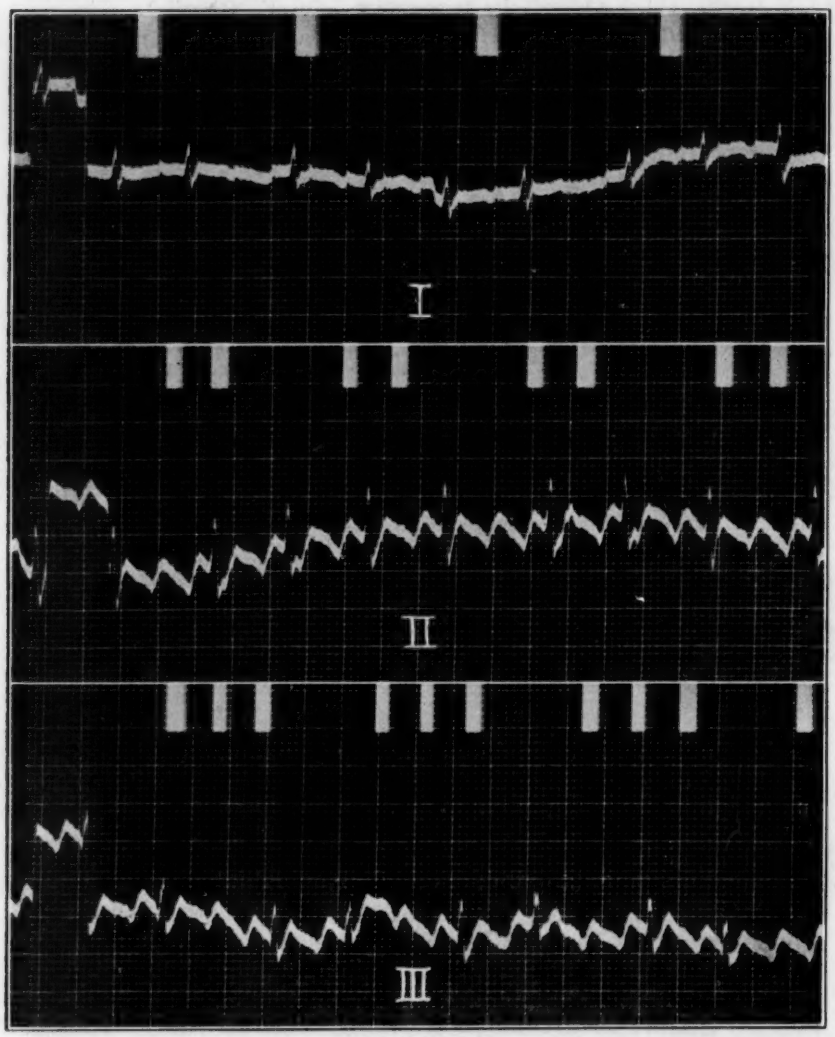

Fig. 2 (Aug. 22, 1945).—An electrocardiogram taken six months later. Ventricular complexes in all leads, especially in lead I, show lower voltage.

twenty-four hours the rate was regular. On September 3 the quinidine sulfate was reduced to 0.1 Gm. every six hours and on September 5 the patient was discharged on a dosage of 0.1 Gm. quinidine sulfate three times daily. During therapy at the hospital daily electrocardiographic readings were obtained.

Two weeks after discharge the patient returned to the pediatric clinic for evaluation. The cardiac findings now consisted of a loud, high-pitched systolic murmur heard over the entire precordium but especially in the fourth left inter-

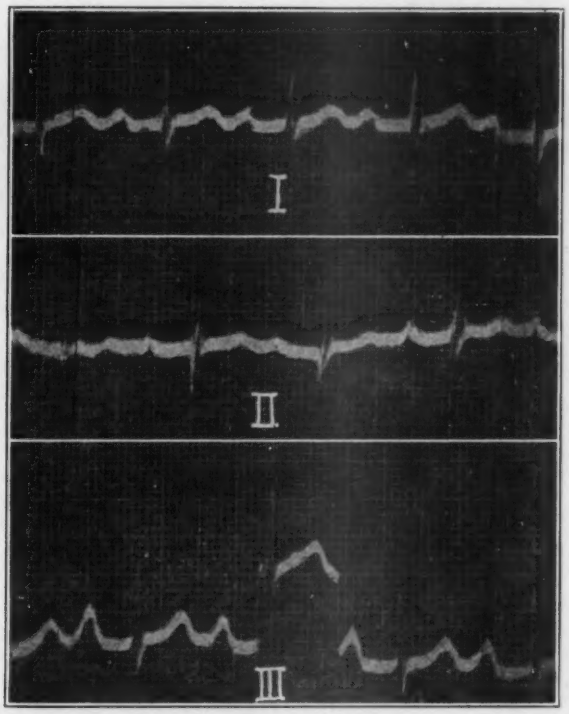

Fig. 3 (Sept. 2, 1945).—An electrocardiogram taken on the third day of quinidine therapy. There are a normal sinus rhythm, a ventricular rate of 100 per minute and a partial heart block. The PR interval is 0.28 second. The shape of QRS has altered in lead II.

TABLE 1.—*Pulse Rate Before and After Therapy with Quinidine Sulfate.*

Dates	Therapy	Pulse Rate	Character of Pulse
2/10/45	None	140	Irregular
8/30/45	None	99 to 120	Irregular
8/31/45	Quinidine sulfate 0.1 Gm. every 3 hours	88 to 120	Irregular
9/ 1/45	Quinidine sulfate 0.1 Gm. every 3 hours	88 to 112	Regular
9/ 2/45	Quinidine sulfate 0.1 Gm. every 3 hours	88 to 99	Regular
9/ 3/45	Quinidine sulfate 0.1 Gm. every 6 hours	99	Regular
9/ 5/45	Quinidine sulfate 0.1 Gm. 3 times daily	92	Regular
9/27/45	Quinidine discontinued	120	Regular
10/26/45	None	100	Regular
11/23/45	None	110	Regular
12/17/45	None	94	Regular

space near the sternum. No enlargement was detected; no thrill was present. The pulse was regular; the blood pressure was 110 systolic and 70 diastolic; the cardiac rate was 110 beats per minute. The gain in weight since institution of therapy was 9½ pounds (4.3 Kg.). The child was seen regularly each week; he remained active and well, and on September 27 the quinidine was discontinued.

He was again admitted to the ward on Nov. 16, 1945, the diagnosis being scarlet fever. He was treated with penicillin and made an uneventful recovery.

During the period of observation and hospitalization results of the Kahn and Mantoux tests were negative, and the urinalysis, sedimentation rate and blood counts were within normal limits.

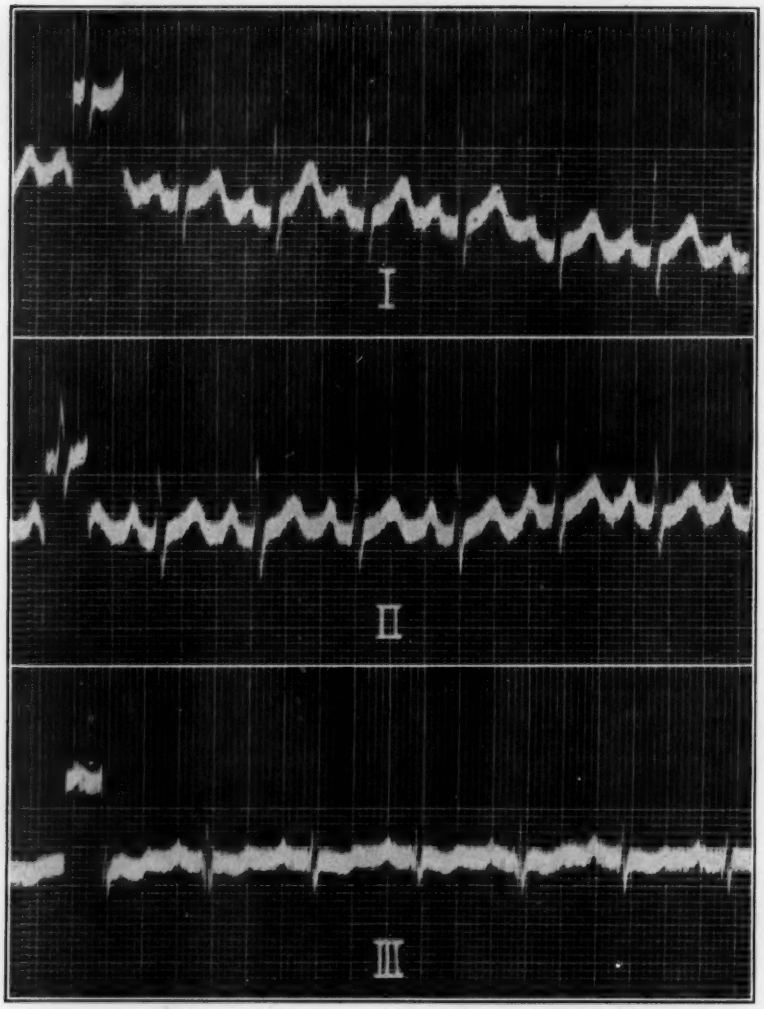

Fig. 4 (Sept. 27, 1945).—An electrocardiogram taken after one month of quinidine therapy. Sinus rhythm is normal. PR interval measures 0.17 second. T waves in leads I and II have increased in height; in lead III they are inverted.

He is being examined periodically, and the cardiac findings (figs. 3, 4, 5, 6 and 7) are remaining the same, with cardiac regularity and with a pronounced apical systolic murmur heard over the entire precordium.

COMMENT

The type of organic lesion present in this case cannot be proved to be congenital. Since the arrhythmia was present at birth or shortly thereafter and remained constant until treated, the diagnosis of congenital heart disease seems likely. Rheumatic fever, either intrauterine [14] or occuring early in infancy,[15] must be considered, and there are some clinical data to suggest this possibility. There is no indication of the arrhythmia resulting from any injury to the chest.[16]

Of the cases which have been reviewed, in only 1 described by Amberg and Willius was there a report of a necropsy to confirm their diagnosis of congenital heart disease. They concluded that the dilatation and hypertrophy of the right auricle reached such a degree as to

TABLE 2.—*Review of Data in Cases of Auricular Flutter*

Author	Age of Patient	Age of Onset	Preexisting Diseases	Duration of Flutter	Treatment	Results
1. Amberg	5 yr.	2½ yr.	Congestive failure	1 mo.	Digitalis	Died
2. Koplik	12 yr.	10 yr.	.....	?	Digitalis	Recurred
3. Poynton	3½ yr.	4 mo.	.....	3 yr.	Digitalis and quinidine	Recurred
4. Carr	Newborn	Before birth	.....	10 days	None	Recovery
5. Sherman	3 mo.	Birth	.....	3½ mo.	Digitalis	Recovery
6. Halbertsma	5 yr.	2 yr.	Congestive failure	3 yr.	Digitalis and quinidine	Recovery
7. Prince et al. (present case)	2½ yr.	Birth	.....	2½ yr.	Quinidine	Recovery

interfere with the orderly function of this chamber, resulting in auricular flutter. Other writers [8] have expressed the opinion that immaturity of the bundle of His may play a part when auricular flutter is present in an infant. Auricular flutter following treatment with digitalis [17] has been reported, and this treatment may have contributed to the presence of the defect in Halbertsma's case.

14. Kissane, R. W., and Koons, R. A.: Intra-Uterine Rheumatic Heart Disease, Arch. Int. Med. **52**:905-910 (Dec.) 1933.

15. Schwarz, H.: An Unusual Case of Acute Rheumatic Fever in an Infant, in Contributions to the Medical Sciences in Honor of Dr. Emanuel Libman by His Pupils, Friends and Colleagues, New York, International Press, 1932, vol. 3, p. 1061-1068.

16. Kahn, M. H.: Auricular Flutter Following Direct Injury to the Chest, Am. J. M. Sc. **179**:605-609 (May) 1930.

17. Wedd, A. M.: Clinical Auricular Flutter, Ann. Clin. Med. **3**:69-92 (July) 1924.

When treatment was necessary in the reports previously mentioned, digitalis was used. Halbertsma also used quinidine sulfate after the arrhythmia had been corrected by digitalis. Sherman gave his patient digitalis for eight days, but the relation of the therapy with digitalis to the appearance of normal rhyhm is difficult to evaluate.

Our patient was given quinidine sulfate 0.8 Gm. daily for three days; then the dosage was reduced to 0.4 Gm. daily. He was discharged on

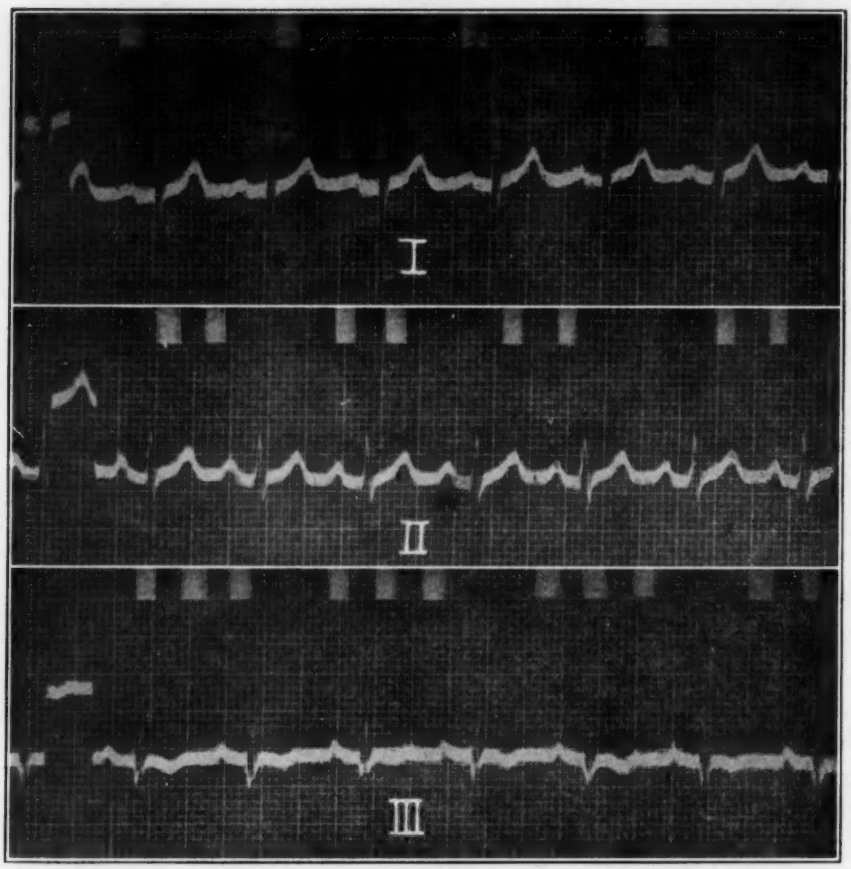

Fig. 5 (Oct. 26, 1945).—An electrocardiogram taken one month after discontinuing the administration of quinidine. Results are like those shown in figure 4.

0.1 Gm. three times a day and remained on this for one month. Within twenty-four hours after the treatment was begun the heart rhythm became regular and the flutter did not recur. As shown by the marked prolongation of the PR interval found in the electrocardiogram (fig. 3) taken the third day after the treatment was begun, the dosage of quinidine was probably larger than necessary.

There is little available information on the dosage of quinidine sulfate needed to correct the different disorders of the cardiac rhythm found in children. Alsever [18] found that in the treatment of paroxysmal auricular tachycardia in infancy and in childhood dosages slightly larger than those calculated by the use of Clark's formula ($\frac{\text{weight of patient}}{150} \times$ average adult dose) or Young's formula ($\frac{\text{age of patient}}{\text{age of patient} + 12} \times$ average adult dose) were needed to produce the desired results. Perhaps these

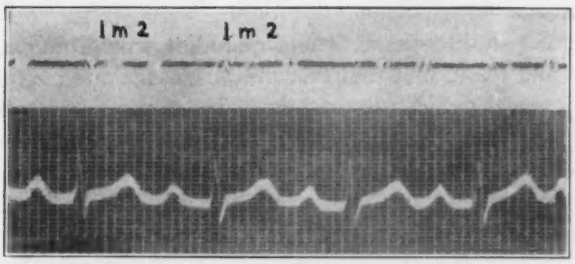

Fig. 6 (Dec. 19, 1945).—Phonocardiogram showing the time of the murmur.

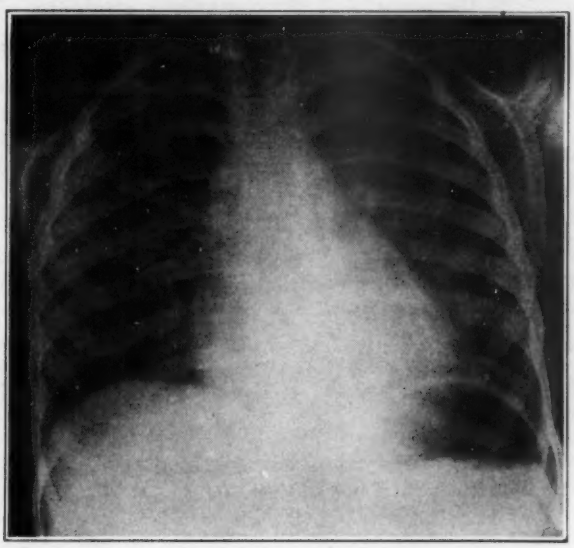

Fig. 7 (Dec. 19, 1945).—A roentgenogram of the chest.

formulas may be applied to the treatment of auricular flutter in children. The maximum daily dose of quinidine sulfate is usually 4 Gm., although a much larger dose is sometimes used. Our patient was 3 years old and weighed 30 pounds (13.6 Kg.) at the time quinidine was given. If one

18. Alsever, W. D.: Treatment of Paroxysmal Auricular Tachycardia in Infancy and Childhood, J. Pediat. **22**:459-467 (April) 1943.

uses 4 Gm. in either of the aforementioned formulas instead of the average adult dose for one day, the correct daily dose for this child would have been approximately 0.267 Gm. The dosage of 0.8 Gm. daily, or about three times the calculated dose, produced decided prolongation of the PR interval during the time it was received. There was no clinical evidence of intoxication, and dramatic results were obtained. It appears from this single case that larger amounts of quinidine than those calculated may be tolerated by children and perhaps may be necessary to correct auricular flutter of long duration.

Messeloff [19] studied the action of quinidine sulfate on the hearts of 12 children and found that the principles of dosage and cumulation governing the clinical use of the drug in children appeared to be identical with those reported for adults. He also noted that children tolerate large doses of quinidine, as judged by the age and weight standards, and expressed the opinion that the usual adult daily dose of 1 to 2 Gm. may be safely given to children.

We attempt to draw no conclusions as to the correct dose or duration of treatment necessary to abolish auricular flutter. We merely offer our comments in the hope that by comparing our case with similar future studies the correct dosage of quinidine sulfate may be more easily determined for use in cardiac arrhythmias of childhood.

SUMMARY

The cases of long-standing auricular flutter present during infancy and childhood have been reviewed.

A case of auricular flutter present since birth or shortly thereafter in a boy 2½ years of age is presented. The patient was treated with quinidine sulfate, and prompt abolition of the irregularity resulted.

The dosage of quinidine sulfate as used in the cardiac arrhythmia of childhood is briefly commented on.

Dr. Morris Weiss interpreted the electrocardiograms and aided in the treatment of this patient.

19. Messeloff, C. R.: Observations on the Use of Quinidine Sulfate in Children, J. Lab. & Clin. Med. **24**:574-580 (March) 1939.

Progress in Pediatrics

CARCINOMA OF ADRENAL CORTEX WITH ADRENOGENITAL SYNDROME IN CHILDREN

Complete Review of the Literature and Report of a Case with Recovery in a Child 8 Months of Age

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NEOPLASM of the adrenal cortex is a fascinating pathologic condition in which little girls become little boys and little boys little men. These little men pass through the "seven ages" of Shakespeare in as many years.

The clinical syndrome produced by active carcinomas of the adrenal cortex has been variously classified by many authors, these classifications depending mainly on the age of the patient affected. The syndrome manifests itself by sexual precocity, with adult size genitalia in boys and early appearance of pubic hair with hypertrophy of the clitoris in girls, each manifestation with its corresponding secondary sexual characteristics.

In this paper we are concerned only with the adrenogenital syndrome as it involves the boy and the girl before the menarche. This paper is further limited to the consideration only of malignant cortical neoplasms which produce the aforementioned syndrome.

The reason for reporting this case is its extreme rarity and its presentation of several unusual features, together with the fact that the patient is the youngest in whom surgical intervention resulted in recovery.

REPORT OF CASE

History.—L. F. was referred to us by Dr. John A. Askin. She was a Jewish girl born July 20, 1944. She first came under our observation on March 29, 1945, at which time she was 8 months of age.

Family History: The mother and father were both normal adults. Both were alive and well. The father had eczema as a child. There was no family history of tuberculosis, cancer, heart disease, disturbances of the kidney or bladder, blood

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dyscrasias, epilepsy, asthma or hay fever. In the prenatal period, the mother exhibited no symptoms of toxemia or anemia. The mother's diet was adequate. The child had a normal full term vaginal delivery. This was the first pregnancy, and the patient is still an only child at the time this is written.

Past History: The birth was normal, the child weighing 6 pounds, 8½ ounces (2,948 Gm.). She had developed normally except for being a long baby and had gained weight. A peeling eczema was present from birth. It apparently itched a great deal, as the child had continually rubbed her arms and legs against the bed-posts. Because of this eczema she had been given a formula of Biolac (a modified milk prepared from whole milk, skimmed milk and lactose, with added thiamine hydrochloride, cod liver oil concentrate and ferric citrate, and the whole homogenized and heat processed) and water. She had also eaten vegetables, beef and chicken. She had not as yet been vaccinated, but she had been immunized against diphtheria. There were no serious illnesses or operations. The only previous illness had been an occasional but not serious cold.

Present Illness: On March 14, 1945 the child was examined routinely prior to receiving immunization to diphtheria. On that date the patient was said to be perfectly well and was given the inoculation against diphtheria. On March 20 the child began to vomit almost everything taken by mouth. The vomitus was sour and orange in color. After the first week, on March 27, the vomiting ceased; but after that date the child did not receive any foods except fluids and the formula—both of which were taken in small quantities. On that day it was noticed for the first time that the abdomen was distended, and that the patient had a temperature of 100 F. A tablet of acetylsalicylic acid was given. It was also noted that "one side of her vagina was swollen." The next day the child's temperature rose to 102 F., and a physician was called. On examination he felt an abdominal mass and stated that the child had an abdominal tumor. The child was then seen by another physician, who confirmed the presence of a mass in the abdomen, and she was sent to the hospital on March 29. There were no associated chills or convulsions. Her bowels were regular throughout her illness, and there was no difficulty in voiding; no hematuria, no apparent dysuria and no menses were observed.

When we saw the child, the eczema was clearing. She did not yet sit up but held her head up, smiled and babbled.

Physical Examination.—The child was a well developed, well nourished white girl not appearing acutely ill or in distress. No hyperpnea or cyanosis was observed. The skin was covered with a healing eczematous lesion—large erythematous patches with occasional crusts.

Head: The head was normal in size and shape. The posterior fontanel was closed, and the anterior fontanel admitted the tip of one finger. No areas of tenderness or of exostosis were present.

Eyes: The pupils were normal and equal and reacted to light. The external ocular muscles were intact and there was no nystagmus. The conjunctivas and scleras were clear. The lids were normal.

Ears: Both drums were intact and appeared as usual, as did the external meatus and the pinna. There was no discharge from the ears except for an excess of cerumen.

Nose: The septum was intact. The mucosa was not inflamed or edematous, and no discharge or crusts were present.

Mouth: No teeth were present. No vesicles or ulcerations of the mucosa were observed. The tongue was as usual both in color and in appearance. The

tonsils were somewhat enlarged but were not inflamed. The pharynx was not inflamed, and no exudate was present.

Neck: There were palpable, shotty cervical and supraclavicular nodes on both sides. The trachea was in the midline. The thyroid was not palpable.

Chest: This was symmetric and expanded equally. The breasts were normal.

Lungs: Both the percussion note and the breath sounds were normal. No rales or rhonchi were present.

Heart: This was not enlarged to percussion. The apex beat was visible, and the point of maximum intensity was at the fourth intercostal space just lateral to the midclavicular line. Sounds were good, the first sound louder than the

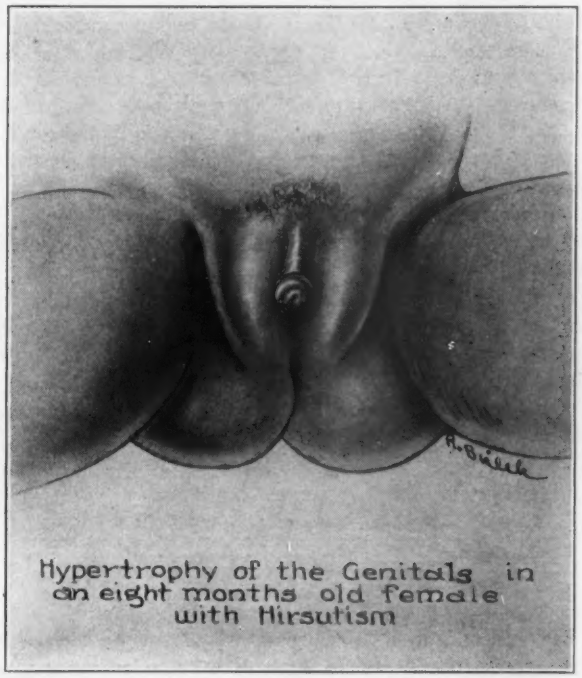

Fig. 1.—Appearance of the genitals in a girl with adrenal carcinoma before an operation was performed.

second and the second pulmonic louder than the second aortic sound. No adventitious sounds were heard. The rate was rapid with regular sinus rhythm.

Abdomen: The abdomen was revealed as distended, more on the right than on the left side. There were no definite palpable masses on the left. On the right there was a firm, smooth, solid mass extending from the costal cartilage down to just below the crest of the ilium, laterally as far as one can go and medially to about 2 cm. from the midline. On ballottement, the mass was found to be palpable posteriorly. The veins over the abdomen were distended, particularly on the right.

Genitalia: There was a definite hypertrophy of the clitoris, although there was all the evidence of a vagina and no evidence of any scrotum. The labia

appeared normal, though the clitoris protruded between the labia majora and measured 3 cm. in length. No vaginal bleeding was observed. Pubic hair was also present (fig. 1).

Extremities: No cyanosis or clubbing was present. Almost all the lymph nodes were enlarged and palpable, though freely movable and not tender.

Weight: At the time of the patient's admission she weighed 15 pounds, 2 ounces (6,860 Gm.).

Laboratory Data.—Urinalysis: At the time of the child's admission, the urine was cloudy, yellow and acid in reaction. There was no evidence of sugar or of albumin. Microscopically, the urine showed occasional granular casts, no red blood cells and 12 to 14 white blood cells per high power field.

Blood Group: The blood group was O.

Blood Count: There were 2,350,000 red blood cells per cubic millimeter, with a hemoglobin content of 6.5 Gm. (40 per cent). White blood cells numbered 13,050 per cubic millimeter. The diffential count was as follows: 1 promyelocyte, 2 myelocytes, 4 juvenile neutrophils, 67 segmented cells and 3 eosinophil forms. There were 22 lymphocytes. Moderate achromia, polychromatophilia and poikilocytosis were observed. There were pronounced anisocytosis and 1 nucleated red blood cell per hundred white blood cells counted.

Analysis of Stool: The stool was soft and yellow and was formed with a small amount of mucus. Results of a test (guaiac) for occult blood were negative, and the microscope revealed no ova, pus or parasites.

Cultures of Material from the Nose and Throat: Hemolytic Staphylococcus aureus predominated, and there was a heavy, deeply pigmented growth. Klebs-Loeffler organisms were not obtained.

Blood Chemistry: A chemical examination gave the following data: urea 27 mg., sugar 116 mg. and chloride (as sodium chloride) 453 mg. per hundred cubic centimeters.

Roentgenography.—Chest: The lungs were clear, and there was no evidence of any metastasis.

Abdomen: A roentgenogram of the abdomen revealed nothing significant.

Bones: The bony and the epiphysial development were normal for the age of the patient.

Intravenous Pyelogram (fig. 2): This showed a double kidney and ureter on the left side. The right kidney was visualized but was incompletely filled. The right kidney was displaced into the pelvis by a large tumor mass. The urine was not examined preoperatively for 17-keto steroids, but the urine was examined for this constituent on the twelfth day after the operation and was found to contain 0.5 mg. per twenty-four hours, which is normal for a child.

Course in Hospital and Operation.—At the time of her admission the patient's temperature was 102 F., and it dropped to 100 F.; thereafter she had a persistent low temperature of 99 to 100 F. Because of a moderate anemia, a transfusion of 200 cc. of citrated blood was given, and this procedure was repeated at the time of operation.

Several consultations resulted in Wilms's tumor, neuroblastoma and a cortical neoplasm being given as possible diagnoses. On April 3 a diagnostic punch was performed, and the material obtained was reported to be mostly necrotic tissue; however, small fragments of intact tissue were suggestive of adrenal cortical carcinoma. Roentgenograms of the lungs did not reveal metastasis, and intravenous pyelograms showed no visualization of the right kidney. The urine and

stools were essentially normal; examination of the blood revealed only a secondary anemia.

On April 6 the child was operated on. An oblique incision was made through the skin, muscles and transversalis fascia in the right lumbar region. An attempt was made to remove the twelth rib, which was only cartilage, and in doing this the pleura was opened. This opening was immediately closed by suturing the tissues to the costal cartilage. The perirenal fat was opened, and then the tumor mass was separated from all its surrounding tissue and finally enucleated, with its capsule, from all tissue as well as from the superior pole of the kidney. The entire mass was removed, and there were no evidences of metastasis into the surrounding tissue. The kidney, which was found in the pelvis, was now pulled up and placed in the proper position. The muscles were sutured with interrupted

Fig. 2.—Intravenous pyelogram made before the operation outlining the tumor mass and the displacement of the right kidney. There is a double kidney on the left with complete reduplication.

surgical gut. The skin was sutured with interrupted black silk. One cigaret drain was placed toward the pleura and one in the perirenal fossa. A moderate amount of bleeding was present. There was little shock; nevertheless, 250 cc. of whole blood was given.

Findings at Operation: A large tumor mass extending from the eighth rib down to and below the crest of the ilium was present. This mass was overlying the superior pole of the kidney (fig. 3). The mass contained a large amount of degenerated tumor tissue with a large amount of blood. The kidney was of normal size and consistency except that it was flattened on the superior pole from the pressure of the tumor. This mass extended beyond the midline medially.

After the operation 2½ rat units of adrenal cortex extract[1] was given twice a day intramuscularly. Postoperatively the child did well except for atelectasis of the lower lobe of the right lung due to the inadvertent opening of the pleura. The immediate postoperative temperature was 104.6 F. rectally, but the patient responded well to the cortical extract and to sulfadiazine. The temperature returned to normal on the third postoperative day. The shock did not appear to be the result of adrenal insufficiency. The child continued to do well but lost 1 pound, 4 ounces (567 Gm.) in the following two weeks. Thereafter her condition improved rapidly. The weight was regained. The blood picture improved with the administration of a solution of crude liver extract and containing thiamine hydrochloride 10 mg., riboflavin 1 mg. and nicotinamide 100 mg. per cubic centimeter (Parentosol B). The patient was discharged from the hospital, much improved, twenty days after the operation.

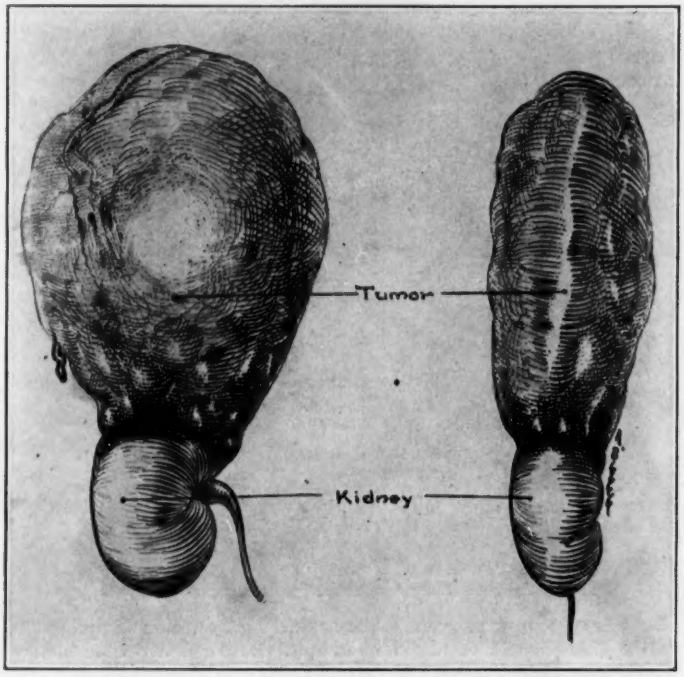

Fig. 3.—The tumor mass in relation to the kidney.

Pathologic Report (Dr. Tobias Weinberg): Grossly the specimen consists of a resected tumor of the right adrenal gland, slightly perforated, measuring 11 by 10 by 5 cm. (fig. 4). It weighs 240 Gm. The tumor mass has a yellowish brown capsule, which is partially covered by adhesions and which contains a number of large blood vessels. On palpation, the tumor mass is found to be soft and almost cystic in consistency. The capsule appears to be intact everywhere. On section, the tumor mass presents a varied appearance; the greater portion is composed of a soft, friable, creamy, gelatinoid material, which is yellowish brown and contains extensive hemorrhagic infiltrations. Some areas are cystic, while

1. The adrenal cortex extract was obtained from The Upjohn Company, Kalamazoo, Mich.

Fig. 4.—A gross specimen of the tumor mass.

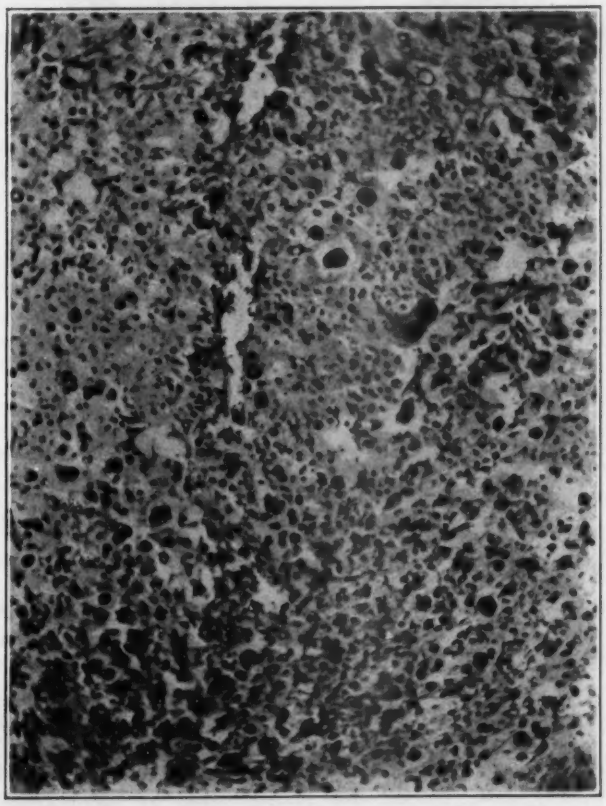

Fig. 5.—A microscopic section of the tumor, showing numerous irregular-shaped giant cells and mitosis.

other areas are composed of a distinctly yellowish, moderately firm tissue, arranged in a streaklike fashion.

Microscopic Report (fig. 5): The sections show a variation in the cellular character of the tumor. In some areas, the cells resemble closely those seen in the glomerulose and fascicular layers of the normal adrenal cortex. However, the majority of the cells are arranged in sheetlike fashion and show a great variation in size and shape. A striking feature is the numerous irregularly shaped giant cells, which contain either one or two large, oval, round or irregularly shaped, hyperchromatic nuclei in a slightly basophilic, finely granular cytoplasm. Many of the nuclei contain large nucleoli. Frequent mitoses, some of which are atypical, are encountered. There are also scattered areas of degeneration and hemorrhage.

Fig. 6.—Intravenous pyelograms made after the operation, showing the replacement of the right kidney.

Subsequent Course: The patient was followed after discharge from the hospital for several months and was seen on Oct. 24, 1945. The mother mentioned that the child had improved considerably and was beginning to act more normally. She had gained about 5 pounds (2.3 Kg.) and was very active. Her appetite was good, and her bowel movements were regular. All hair had disappeared from the suprapubic region, but there was still some on her face. The eczema of the skin had entirely disappeared. The clitoris was still enlarged, measuring over 1 cm. in length, but it was now necessary to separate the labia majora to observe the clitoris. Intravenous pyelograms (fig. 6) were made, and they revealed the dye appearing in normal time in both kidneys. There was evidence of a double kidney on the left. The pelves, calices and ureters were normal in size and shape but somewhat incompletely outlined. The right kidney was

in its normal position. When last seen on Oct. 31, 1946 she weighed 25 pounds (11.3 Kg.) and was 34 inches (86 cm.) tall. The clitoris was about the same size but was visible only on separation of the labia majora. She appeared to be in excellent health.

SUMMARY

A carcinoma of the right adrenal cortex was observed in an infant 8 months of age, with an enlarged clitoris, a palpable abdominal mass and the presence of hirsutism. An operation was performed, with successful removal and full recovery of the patient.

OTHER CASE HISTORIES

A thorough search of the world's literature has been made in order to bring up to date all the data reported concerning malignant adrenal cortical neoplasms associated with the adrenogenital syndrome in children. All the cases reported in the literatue have been digested in the following summaries of cases. Many other cases have been closely studied, but 54 were considered proved instances of malignant adrenal cortical neoplasm producing the syndrome in question in both sexes.

I. Cases in Which Operation Was Successful.—CASE 1.—Collett (1924) reported the case of a girl who was normal at birth. At the age of 6 to 8 months hair developed on the genitalia, and at the age of 1 year this extended over the trunk and extremities. Her voice was deep. No menses were present. She was fat, her weight being 15.1 Kg. while her height was 80.75 cm. An indirect laryngoscopy revealed vocal cords like those of a man. The labia majora and the mons veneris were hypertrophied. The clitoris was 1.5 cm. in length. She had a redundant prepuce with a groove on the under surface. The uterus was normal, and no prostate was palpable. The mammae were also normal. Examination of the bones revealed no abnormality. A palpable abdominal mass was present on the left side.

One year was allowed to pass before an operation was done because the physicians in charge "considered the risk too great at so early an age." In May 1921, when the child was 1½ years of age, an operation was performed, and an adrenal tumor 3.5 by 2.5 by 2.2 cm., weighing 10 Gm., was removed. A diagnosis of hypernephroma was made. An examination in August 1922 revealed the skin to be smooth and more childlike; less fat was present. The labia and mons veneris were smaller, and the voice was not so hoarse. Another examination was made in May 1923. Hair was still present on the labia, and the voice was still deep. The patient was feeling well. No recent communication has been available in the follow-up of this case.

CASE 2.—Fordyce and Evans (1929) reported the case of a girl aged 2 years, who was normal at birth. Soon thereafter, hair was present on the upper lip. An abdominal tumor became palpable. The labia were large, and the clitoris was 3 cm. long. Hair was present on the genitalia. The diagnosis of left hypernephroma was made. An operation was performed in August 1927, and an encapsulated hypernephroma was removed weighing 1,500 Gm. and 14 by 11 cm. The patient was reexamined in December 1928 and was found to be in good health. The clitoris was smaller, and the pubic hairs were gone. A personal communication about the subsequent course in this case was obtained on April 13, 1946. Nineteen years after the operation the patient was found to be a perfectly normal young woman.

CASE 3.—Harris and Plewes (1930) reported the case of a girl aged 3 years and 10 months. She was normal at birth. Her symptoms began at 3 years of age with abdominal pain. The clitoris was 1.9 cm. in length and had a ventral groove. The clitoris became larger and grew to 3.8 cm. in length. She had a husky voice and pubic hair. An abdominal mass was palpable on the left side, causing pressure on the stomach, as revealed by a roentgenogram, and a diagnosis of hypernephroma was made. She was operated on in June 1929, and a hypernephroma of the left adrenal gland 12 by 6.5 cm. was found. The patient was reexamined in ten months. Her voice was improved, although the pubic hair and clitoris were unchanged. There was no evidence of recurrence of the tumor. A personal communication was received that this child died shortly after the reexamination in 1930, but an autopsy was not done.

TABLE 1.—*Analysis of Cases*

Case No.	Author and Year	Sex	Condition at Birth	Age at First Symptoms, Yr.	Age at Operation, Yr.	Size of Genitalia			Age at Appearance of First Menses, Yr.	Body Development	Breasts	Voice Changes	Pubic Hair*
						Clitoris, Penis, Cm.	Labia or Scrotum	Uterus, Ovaries or Testes					
1	Collett 1924	F	Normal	½	1½	1.5	Hypertrophic	Normal	None	Obese	Normal	Deep	+
2	Fordyce and Evans 1929	F	Normal	..	2	3	Large	.....	.....	.....	.....	.....	+
3	Harris and Plewes 1930	F	Normal	..	3⅚	3.8	.....	.....	.....	.....	.....	Husky	+
4	Walters, Wilder and Kepler 1934	F	Normal	4	8	...	Precocious	.....	8, every 2 months	Obese	Developed	Coarse	+
5	Reilly, Lisser and Hinman 1939	F	Normal	1½	2	2.5	Enlarged	Normal	None	Like a 3½ year old	Normal	Deep	+
6	Gross 1940	F	Normal	2 wk.	3½	3.8 by 0.96	Large	.....	.....	Masculine	Normal	Deep	+
7	Pratt and Schaefer 1945	F	Normal	2⅔	2¾	Like a penis	Large	Normal	.....	Muscular	.....	Deep	+
8	Goldstein and Rubin 1946	F	Normal	⅔	⅔	3	Enlarged	Normal	None	Large and strong	Normal	Normal	+

* Explanation of symbols: + indicates presence of hair; — indicates absence of hair, and .. indicates no mention of

CASE 4.—Walters, Wilder and Kepler (1934) reported the case of a girl aged 9 years whose condition was diagnosed as a "cortical adenoma"; the same case was reported by Walters and Kepler in 1938 as a "cortical carcinoma." The girl's birth and development were normal. At the age of 4 years the breasts developed, and hair was noticed over the body. The voice became coarse. At the age of 5 pubic hair was present. At the age of 8 the menses started, lasting for four days and thereafter recurring at two month intervals. There was also present obesity of the trunk, neck and face. Hirsuties was present on the face, body, pubes and axillas. The breasts were precocious, as were the external genitalia. There was acne of the face and trunk. The blood pressure was elevated: 133 systolic and 97 diastolic. The osseous age was that of a 12 year old. Operation was done in October 1933, and a tumor of the left adrenal gland, 6 by 4 by 2 cm., a portion of which projected into an enlarged adrenal vein, was removed. The right adrenal gland was half the normal size, but normal histo-

logically. Three weeks after the operation the child's weight had decreased, and some hair had fallen out. Later the menses ceased and the skin became smooth. The voice became of a higher pitch, and the breasts and genitalia were smaller. The patient was examined in March 1934, and she was found to be well, but the genitalia were almost of adult size, although the clitoris was smaller than it had been. The patient was reexamined in August 1937 (four years later). Menses had reappeared twenty-two months after the operation and had been regular and normal since. She appeared normal except for large and adipose breasts. The genitalia were normal and of adult type. The clitoris had receded and while large was not huge. The hirsutism and acne had gone. The blood pressure was lower, around 110 systolic and 72 diastolic. This patient was last examined in 1941, eight years after the operation and was feeling well.

h Operation Was Successful.

rsuties *		Palpable Abdominal Mass, Side	Preoperative Diagnosis	Therapy	Tumor		Histologic Observations	Metastases	Postoperative Diagnosis, Side	Result
s Beard	General				Size, Cm.	Weight, Gm.				
..	+	Left	Adrenal tumor	Removal	3.5 by 2.5 by 2.2	10	Adrenal hypernephroma	None found	Hypernephroma of left adrenal gland	2 years later well, 1923
..	+	Left	Adrenal hypernephroma	Removal	14 by 11	1,500	Adrenal hypernephroma	None found	Hypernephroma of left adrenal gland	19 years later well, 1946
..	..	Left	Adrenal hypernephroma	Removal	12 by 6½	..	.....	.....	Hypernephroma of left adrenal gland	10 months later well, 1930
+	+	..	.....	Removal	6 by 4 by 2	..	Adrenal hypernephroma	Projected into the vein	Hypernephroma of left adrenal gland	8 years later well, 1942
—	—	Left	Adrenal tumor	Removal	12 diam.	..	Carcinoma of zona fasciculata	.....	Hypernephroma of left adrenal gland	5 years later well, 1942
..	..	None	Adrenal tumor	Removal	7½ by 6½ by 4	110	.....	.....	Hypernephroma of right adrenal gland	8 months later well, 1940
..	..	..	Adrenal cortical tumor	Removal	5.5 by 4.5 by 3.3	48	Adrenal cortical carcinoma	No evidence	Carcinoma of right adrenal gland	6 years later well, 1944
—	—	Right	Adrenal cortical carcinoma	Removal	11 by 10 by 5	240	Adrenal cortical carcinoma	None found	Carcinoma of right adrenal cortex	1¾ years later well, 1946

tory of the case reported.

Case 5.—Reilly, Lisser and Hinman (1939) reported the case of a girl aged 2 years who was normal at birth. At the age of 15 months, adhesions were present between the labia. At 22 months there were pubic hair and an enlarged clitoris 2.5 cm. long. Her voice was deep. She was large, like a 3½ year old child, and had an osseous age of 4. The pyelogram showed that the left kidney was low, with a blunting of the calices. An abdominal mass was palpable, and a preoperative diagnosis of adrenal tumor was made. The blood pressure was 115 systolic, 65 diastolic. Operation was performed, and the left oblique lumbar extraperitoneal approach was utilized. A mass 12 cm. in diameter was found, and the diagnosis of carcinoma of the adrenal cortex was made. Three months postoperatively roentgenotherapy was instituted but caused nausea, vomiting and leukopenia. The clitoris and hirsuties were regressing. Seven months after the operation the pubic hair disappeared and the clitoris was smaller. Reexamination after two years revealed no pubic hair, a smaller clitoris and slowed body and bone

growth. There were no secondary growths clinically, and the kidney was in a normal position. The blood pressure was now 102 systolic and 40 diastolic. At the age of 7 years the patient was still in good health as reported by Reilly (1942).

CASE 6.—Gross (1940) reported the case of a girl aged 3½ years who was normal at birth. At the age of 2 weeks a prominence of the vulva, with a few pubic hairs was noticed. In the first year, the clitoris increased in size and finally reached 3.8 cm. in length, with a glans 0.96 in both length and diameter. The labia were also large. The breasts were not enlarged. Masculinization was pronounced with a precocious body growth, a deep voice, acne and hypertension (blood pressure, 110 systolic and 70 diastolic). The osseous growth was like that of a child of 9 or 10 years. The concentration of urinary androgen was high, as was that of urinary estrogen. No abdominal masses were palpable. A roentgenogram showed a mass in the right side of the abdomen, and an intravenous pyelogram showed displacement of the right kidney downward to a slight degree. An operation was performed, and a neoplasm of the right adrenal gland weighing 110 Gm. and measuring 7.5 by 6.5 by 4 cm. was found. Postoperatively, the urinary androgen and estrogen fell. Examination eight months after the operation showed the acne to be gone and the clitoris shrunken. The appearance was more feminine, but the pubic hair and the voice remained unchanged. Four months after this examination, the child died under anesthesia given for a simple tonsillectomy.

CASE 7.—Pratt and Schaefer (1945) reported the case of a 2¾ year old girl. Her birth and development were normal until one month prior to her being brought to the physician. It was at this time that the mother noticed an unnatural swelling of the genitalia, development of pubic hair and rapid growth. Physical examination revealed masculine muscular development, pubic hair and an enlarged clitoris which protruded between relatively large labia minora. The tip of the clitoris resembled a glans penis. The labia majora were enlarged. A roentgenogram of the skull revealed a normal sella turcica. There was advanced osseous development. A bioassay of the urine failed to reveal estrogens or androgens. The child was observed for six months, during which time she increased 6 inches (15 cm.) in height (height 39 inches [99 cm.]) and gained 12 pounds (5.4 Kg.) (weight 36 pounds [16.3 Kg.]). Her voice was deeper, and hair appeared in the axillas. The external genitalia became more conspicuous. A diagnosis of virilism and of adrenal cortical tumor was made. In January 1938, an operation was performed through a right rectus incision. The ovaries, tubes and uterus were normal. The left adrenal gland was normal. From the right adrenal gland a well encapsulated mass was removed through an incision in the peritoneum. It weighed 48 Gm. and measured 5.5 by 4.5 by 3.3 cm. The histologic impression given was of a cortical adrenal carcinoma. The postoperative course was uneventful. There was no evidence of metastasis. The general physical development had become more feminine, and the patient had continued development in this direction when last observed, six years after the operation.

CASE 8.—Goldstein and Rubin (1946): This report is our case previously described in this paper.

II. Cases of Unsuccessful Surgical Intervention.—CASE 9.—Dobbertin (1900) reported the case of a girl aged 14 months who was born with a tumor in the abdomen. There was hair on the labia majora, body, cheeks and chest. The genitalia were not described. The child was well nourished. At operation, a tumor was found to have replaced the left adrenal gland. Both the tumor and the left kidney were removed at operation. Postmortem examination revealed secondary growths behind the manubrium sterni. The mass was described as a "congenital carcinoma."

CASE 10.—Miller (1903) reported the case of a girl aged 2 years who was normal at birth. The symptoms started at the age of 1½ years, with abdominal swelling, hypertrophy of the labia minora and labia majora and the presence of pubic hair. The clitoris at the time of operation was 2.5 cm. in length. Later it grew to 4 cm. with a retractable prepuce (Glynn). The operation revealed a vascular tumor of the right adrenal gland. Removal was not attempted. The patient survived and went through an attack of measles and bronchopneumonia, dying eleven months later (from exhaustion [Glynn]). The intervening period and the postmortem examination were reported by White and Nisbet. She was described as a child resembling a "little old woman," with a thick neck, prominent eyes and dark skin. The clitoris at this time was 4 cm. in length with a prepuce. There was hair on the pubis. Secondary growths were found in the liver, mesenteric nodes and the right lung; the tumor was described as a hypernephroma.

CASE 11.—Linser (1903) reported the case of a boy aged 5 years and 7 months at death. Symptoms started at the age of 1¼ years. He was normal at birth. Later he resembled a youth of 16 to 18 years. His weight was 38 Kg. He had twenty-eight teeth. All eight carpal ossifications were present. He had had hair on his pubis for one year. His penis was 8 to 9 cm. long and 12 to 14 cm. in erection. The testes were the size of a pigeon's eggs, but there was no spermatogenesis. Sexual activity was present, according to Glynn. A tumor was palpable in the region of the left kidney. At operation no attempt was made to remove the mass. A postmortem examination revealed a large tumor of the left adrenal gland which had ruptured into the vena cava, and secondary growths were also found in the lungs. The thyroid, pineal and hypophysial glands were normal. No thymus was found. The tumor was reported as a hypernephroma.

CASE 12.—Adams (1905) reported the case of a boy aged 14⅓ years who was normal at birth. Symptoms began at 10 years of age. He was described as "a sturdy little man" of great muscular strength. He had a beard at the age of 2 years. A tumor was palpated in the left side of the abdomen. An exploratory laparotomy revealed an inoperable tumor in the region of the left kidney. Death occurred seventeen months later. A tumor of the left adrenal gland was found which weighed 3,900 Gm. and was encapsulated. The kidney was not involved. Secondary growths were found in the spleen and the liver, which was very large, weighing 15½ pounds (7.3 Kg.). The right adrenal gland was normal. The tumor was reported as a malignant hypernephroma (perithelioma).

CASE 13.—French (1912) reported the case of a girl aged 7 years who had pubic hair at 18 months of age. The external genitalia were hypertrophied. No menses were present. A tumor was palpable in the left part of the abdomen, and a diagnosis of tumor of the adrenal gland was made. At the time of operation the tumor and the left kidney were removed, though the kidney was free from any growth. She had secondary growths in the lung, and died shortly after the operation. This was reported as a perithelioma-hypernephroma (Glynn).

CASE 14.—Jump, Beates and Babcock (1914) reported the case of a girl aged 7 years, a twin, who was normal at birth. At the age of 1 year she showed great physical development and great strength. At 7 years, she was 53 inches (135 cm.) tall and weighed 90 pounds (40.8 Kg.). She had a deep voice and a larynx like a man. Mentally, she was well developed. There was hair on the pubes, legs, trunk, face and axillas. The labia were large. The clitoris was 2.5 cm. in length and grooved on the under surface. The breasts were not enlarged. No menses occurred. A palpable tumor was present in the right

TABLE 2.—*Analysis of Cases in*

Case No.	Author and Year	Sex	Condition at Birth	Age at First Symptoms, Yr.	Age at Operation, Yr.	Size of Genitalia			Age at Appearance of First Menses, Yr.	Body Development	Breasts	Voice Change
						Clitoris, Penis, Cm.	Labia or Scrotum	Uterus, Ovaries or Testes				
9	Dobbertin 1900	F	Mass present	..	1⅙	...	.....	.....	.....	Well nourished	.....	.....
10	Miller 1908	F	Normal	1½	2	4	Hypertrophic	Ovary large	None	Like little old woman	Normal	.....
11	Linser 1908	M	Normal	1¼	5 7/12	8 to 9 erect 12 to 14	.....	Pigeon eggs	.....	Like a youth 16 to 18	.....	.....
12	Adams 1905	M	Normal	10	14⅓	...	.....	.....	.....	Sturdy little man	.....	.....
13	French 1912	F	....	1½	7	...	Hypertrophic	.....	None	.....	.....	.....
14	Jump, Beates and Babcock 1914	F	Normal	1	7	2½	Large	Infantile	None	Great body development	Not large	Deep
15	Van den Bergh 1915	F	....	..	3	Very big	Large	.....	None	Tall and heavy	.....	.....
16	Schiff 1918	F	....	1¾	2	Normal	.....	Normal	.....	Adipose	Normal	Heavy
17	Ambrozic and Baar 1920	F	....	1	3	Like a little finger	.....	Normal	.....	Like 6 year old	Underdeveloped	Heavy
18	Hoag 1923	F	Normal	3	4¼	2.2	Hypertrophic	.....	None	Normal	.....	.....
19	Gibbon 1924	F	....	2⅔	3	Pronounced enlargement	.....	Infantile	None	.....	.....	.....
20	Kennedy and Lister 1927	F	....	13	13½	...	Hypertrophic	Infantile	None	"Fat little old woman"	.....	.....
21	Ruitinga 1928	F	....	..	4	Large, like a penis	Hypertrophic	.....	.....	Like a child of 12 years	Normal	.....
22	Fordyce and Evans 1929	M	Normal	½	2	Large	.....	Enlarged	.....	Strong	.....	.....
23	Van der Bogart 1933	F	Normal	¾	2	Very large	Prominent	.....	.....	Fat	.....	.....
24	Quinby 1933	M	Normal	⅝	12	Slight enlargement	.....	.....	.....	Looked 17	.....	Deep
25	Pitroeffy Szabó	F	Normal	½	3½	Normal	.....	Normal	.....	Obese	.....	Deep
26	da Roche 1939	F	Normal	..	2½	Slight enlargement	Hypertrophic	.....	.....	Precocious	.....	Hoarse
27	Gross 1940	M	Normal	2⅔	3	Like that of an "adolescent youth"	.....	.....	.....	Like a boy of 11	.....	Deep
28	Albert 1941	F	....	2	2	Slight enlargement	.....	Small	.....	Wasted and puny	Small	.....
29	Taylor and Wiseman 1942	M	Large abdomen	Birth (?)	11/12	3 times normal size	Hypertrophic	Large	.....	Appeared older	.....	.....
30	De Jaeger 1942	F	Anomalous genitals	Birth	8	Hypertrophic "small penis"	Hypertrophic	Small	Mild, at 1¼	Strong and large: 12th year ossification at wrist	Not developed	Deep
31	Kempton and Lohr 1942	F	Normal	½	1¼	Enlarged	Hypertrophic	.....	.....	Grew rapidly	.....	Heavy

...rsuties		Palpable Abdominal Mass, Side	Preoperative Diagnosis	Therapy	Tumor		Histologic Observations	Metastases	Postoperative Diagnosis, Side	Outcome
Beard	General				Size, Cm.	Weight, Gm.				
+	+	Left	.....	Removed kidney and mass	..	..	Giant cells	Behind manubrium sterni	Hypernephroma of left adrenal gland	
..	..	Right	.....	Exploratory laparotomy	..	..	.....	Liver, right lung, mesenteric nodes	Hypernephroma of right adrenal gland	Died 11 months later from exhaustion
..	..	Left	.....	Exploratory laparotomy	Large	..	.....	Vena cava and lungs	Hypernephroma of left adrenal gland	Tumor inoperable
+	..	Left	.....	Exploratory laparotomy	..	3,900	Perithelioma	Spleen and liver	Hypernephroma of left adrenal gland	Tumor inoperable
..	..	Left	Tumor of adrenal gland	Removed kidney and mass	..	..	Perithelioma	Lung	Hypernephroma of left adrenal gland	Death from metastasis in lung
+	+	Right	Tumor of adrenal cortex	Removed	..	..	.....	None found	Hypernephroma of right adrenal gland	Died from operation
..	..	..	.....	Removed	22 by 16 by 12	2,000	.....	.....	Hypernephroma of left adrenal gland	Died from operation
+	..	Right	Hypernephroma	Exploratory laparotomy	16 by 11 by 6	..	.....	None found	Hypernephroma of right adrenal gland	Died from operation
..	+	Left	Malignant adrenal tumor	Removed	..	..	.....	Lung and brain	Hypernephroma of left adrenal gland	Died from operation
+	..	Right	Malignant hypernephroma, cranial metastasis	Removed	..	..	.....	Lungs and liver; no cranial metastasis	Hypernephroma of right adrenal gland	Died from operation
+	+	Left	Adrenal tumor	Removed	13 in. diam.	720	Hypernephroma	None found	Hypernephroma of left adrenal gland	Died from operation
..	+	Left	.....	Removed	21.6 by 12.7 by 7	..	.....	Lung	Hypernephroma of left adrenal gland	Died from operation
+	..	..	Carcinoma of the left adrenal gland	Exploratory laparotomy	Small cocoanut	..	.....	.....	Carcinoma of left adrenal gland	Died from operation
+	+	..	Cortical hypernephroma	Removed	6 by 4.4 by 3.4	66	.....	Liver and brain	Hypernephroma of left adrenal gland	Died from operation
+	+	Right	.....	Removed	9 by 6 by 7	79.7	.....	.....	Hypernephroma of right adrenal gland	Died from operation
+	..	..	Acute condition in the abdomen	Exploratory laparotomy	..	..	Adrenal carcinoma	Liver, lungs, renal and inferior vena cava	Hypernephroma of right adrenal gland	Died from abdominal hemorrhage
+	+	..	.....	Exploratory laparotomy	Child's head	707	Hypernephroma of adrenal cortex	.....	Hypernephroma of right adrenal gland	Died from operation
..	+	Right	Congenital tumor of adrenal gland	Exploratory laparotomy	..	..	.....	Adherent to liver	Carcinoma of right adrenal gland	Died from operation
..	..	Left	Adrenal neoplasm	Removed	..	640	.....	.....	Carcinoma of left adrenal gland	Died of shock
..	..	Right	Adrenal cortical tumor	Removed	22.8 by 15.2	..	Cellular malignant tumor	Diaphragm, inferior vena cava, abdominal glands	Carcinoma of right adrenal gland	Died of shock
—	—	Left	Adrenal tumor	Removed	10 by 10 by 7	..	Anaplasia	.....	Carcinoma of left adrenal gland	Died from operation
+	+	..	Tumor of adrenal gland	Removed	Chicken egg	..	Adrenal cortical carcinoma	.....	Carcinoma of right adrenal gland	Died 1 month after operation of shock and collapse
+	+	..	.....	Removed	13 by 10 by 7	610	Adrenal carcinoma	.....	Hypernephroma of left adrenal gland	Died from operation

side of the abdomen, and a diagnosis of tumor of the right adrenal cortex was made. Removal was attempted, but the patient died three hours later. A postmortem examination was done, and involvement of the right kidney without demarcation was revealed. The left adrenal gland was normal. The uterus and ovaries were infantile. No secondary growths were found. The tumor was reported as being a hypernephroma.

CASE 15.—Van den Bergh (1915) reported the case of a girl aged 3 years who showed "premature development of secondary sexual characteristics" and of the external genitalia. No menses occurred. An operation was performed, and a tumor of the left adrenal gland was removed. It weighed 2 Kg. The patient died postoperatively of shock. The tumor was reported as a carcinomatous hypernephroma.

CASE 16.—Schiff (1918) reported the case of a girl aged 2 years. She had had symptoms for two and one-half months. She had a ravenous appetite, a heavy voice and adiposity. She weighed 11.6 Kg. and was 74 cm. in height. She had hair in the pubic region (3 cm. long) and a beard. The breasts and genitalia were normal. An abdominal tumor was palpable on the right side and a diagnosis of hypernephroma was made. An exploratory laparotomy was done, which was followed by the patient's death. Postmortem examination revealed a tumor of the right adrenal gland, 16 by 11 by 6 cm., separate from the kidney. The thymus, the left adrenal gland, the uterus and the ovary were normal. The hypophysis and the epiphysis were slightly enlarged. There was scanty colloid present in the thyroid glands. No secondary growths were noted. The tumor was reported as a hypernephroma.

CASE 17.—Ambrozic and Baar (1920) reported the case of a girl aged 3 years. Symptoms started at the age of 1 year. She had a mannish voice, looked as if she were 6 years of age and was mentally precocious. Her height was 105 cm. and her weight 18.3 Kg. The muscles were well developed, and eight ossification centers were present in the wrist. The labia were large and lipomatous. The clitoris was like a little finger and was grooved on the under surface. The breasts were undeveloped. There was hair on the pubes, labia majora and arms, but it was scanty in the axillas. A tumor was palpable in the left side of the abdomen, and a diagnosis of malignant tumor of the adrenal gland was made. At operation the tumor and the left kidney were removed. Death occurred that night. A postmortem examination revealed the internal genital organs to be normal except for a cervix and vagina larger than usual. Other endocrine organs were normal. A cyst of the pineal gland was present. Secondary growths were found in the lungs and in the right temporo-occipital lobe of the brain. The tumor was encapsulated and was reported as a hypernephroma.

CASE 18.—Hoag (1923) reported the case of a girl aged 4¼ years who was normal at birth. There was normal development mentally and somatically. At the age of 3, there was hair present on the pubes; the eyebrows were heavy as well as the scalp. The upper lip, chin and axillas were also hirsutic. The nutritional state was excellent. A mass was palpable on the right side of the abdomen. The labia majora and minora were hypertrophied. The clitoris was 2.2 cm. in length, with a redundant prepuce. The patient was admitted to the hospital in a coma. She had three generalized convulsions, and a diagnosis of malignant hypernephroma was made, with possible intracranial secondary growths. Intraperitoneal inflation with carbon dioxide gas was performed, and this revealed a shadow above and to the right of the renal shadow. Roentgenograms of the

skull failed to reveal any secondary growths. The child's height was 96 cm. and her weight 34.5 pounds (15.7 Kg.). Her voice was deep. An operation was performed, and a tumor of the right adrenal gland, which was encapsulated, globular and friable, was found. This was not completely removed. The patient died four hours after the operation. A postmortem examination revealed the thymus and the left adrenal gland to be hypoplastic. The thyroid was normal, as were the uterus and the ovaries except for many large cystic follicles. No menses had occurred. Secondary growths were present in the lungs and in the liver. The pineal and pituitary gland were normal.

CASE 19.—Gibbon (1924) reported the case a girl aged 3 years. Four months prior to the patient's hospitalization, an enlarged abdomen was noticed. There was an excess of hair on the pubes, labia, axilla, back and face, as well as overgrown eyebrows and a downy growth on the upper lip. No menses had occurred. The clitoris was greatly hypertrophied. The uterus and ovaries were infantile. Examination of the thyroid and thymus revealed nothing significant. The Wassermann reaction was negative. A roentgenogram of the skull showed no abnormality. An abdominal mass was palpated in the left upper quadrant. Carbon dioxide gas was injected intraperitoneally, and by means of this a mass at the upper pole of the left kidney was revealed. No secondary growths were found in the lung. The patient was operated on transperitoneally. The tumor was separated but was ruptured. The patient died twenty hours after operation, with a temperature of 105 F. and a respiratory rate of 60. An encapsulated mass 13 cm. in diameter, weighing 720 Gm., was removed and histologically was found to be a hypernephroma.

CASE 20.—Kennedy and Lister (1927) reported a case of a girl aged 13½ years. She was a fat child and had grown fatter during the last six months. She was 4 feet, 6 inches (137 cm.) tall and weighed 6 stone 12 pounds (96 pounds) [43.5 Kg.]. She had a face like a "stout little old woman." She had hair on her back and shoulders, and pubic hair was also abundant. No menses had occurred. The genitalia were slightly hypertrophied. A mass was felt in the left side of the abdomen. An operation was performed, and a tumor of the left adrenal gland was removed. Thirty-six hours after the operation she went into shock and died. The tumor was 21.6 by 12.7 by 7 cm. and weighed 1,700 Gm. Secondary growths were found in the right lung. The uterus was infantile. No other abnormalities were found.

CASE 21.—Ruitinga (1928) reported the case of a girl aged 4 years who had the appearance of a 12 year old child and who weighed 29 Kg. (normal, 16 Kg.). Hair was present on the cheeks, upper lip, chin, arms, legs and pubic region. A discharge was present from the genitalia. The labia majora were conspicuously enlarged, and between them was a very large clitoris, giving the impression of a penis formation with hypospadias. The breasts were not enlarged. Pyelography showed that the adrenal gland was pressing on the left kidney. A diagnosis of carcinoma of the left adrenal gland was made. An exploratory laparotomy was performed through a left-sided incision with the intention of seeing whether or not metastasis was present in the liver. The stomach, spleen, colon and intestines were all adherent and bound down. The retroperitoneal area was palpated, and a round growth the size of a small coconut and not connected with the kidney or stomach was revealed which was easily movable and had not grown into the surrounding tissues. The patient never regained consciousness, and she died twenty-four hours later. Pathologic and anatomic diagnosis showed a carcinoma of the left adrenal gland.

CASE 22.—Fordyce and Evans (1929) reported the case of a boy aged 2 years who was normal at birth. At the age of 6 months pubic hair was present, and the penis was large. At 8 months of age an acne rash was present on the back. He was extremely strong, weighed 38 pounds (17.2 Kg.), and was 2 feet, 10 inches (86.4 cm.) tall. He had hair on his chin, upper lip, cheek, breasts and axillas. Both testicles were enlarged, and the penis was like that of an adult. The diagnosis of hypernephroma of the left adrenal cortex was made. The patient was operated on, and the diagnosis was confirmed. Death occurred twelve hours after the operation. The tumor was 6 by 4.4 by 3.4 cm. and weighed 56 Gm. The right adrenal gland was small. No spermatogenesis was found. Examination of the prostate gland showed fibrous tissue and muscle in excess. Secondary growths were present in the liver and in the brain.

CASE 23.—Van der Bogart (1933) reported the case of a girl of 2 years who was normal at birth. At the age of 9 months she became extremely fat, and hair was noticed on the body and pubes. Her eyebrows were heavy. She had a mustache, and the hair of the scalp descended onto the forehead. She had a prominent vulva. The clitoris was extremely large. A mass was palpated in the right side of the abdomen. An operation was performed, and a right adrenal carcinoma 9 by 6 by 7 cm., weighing 79.7 Gm., was removed. The patient died thirty-six hours postoperatively.

CASE 24.—Quinby (1933) reported the case of a boy of 12 years who was healthy until the age of 10 months, when pubic hair and enlarged genitalia were noticed. His voice was deep. At the age of 5 years, he was 48 inches (122 cm.) tall and weighed 53 pounds (24 Kg.). His genitalia were fully developed, but at the age of 11 years he looked like a boy of 17 and had a pronounced beard. He was operated on for an acute condition within the abdomen, and a large retroperitoneal tumor with intra-abdominal hemorrhage was found. Seventeen days later, he was operated on again. A preoperative diagnosis was now made of an adrenal cortical neoplasm which had caused intra-abdominal hemorrhage. The mass was too large to remove, and the blood supply to the mass was therefore ligated. Nevertheless, he bled heavily and died twelve hours after the operation. Postmortem examination revealed a carcinoma of the adrenal cortex, with secondary invasion of the liver, renal vein, inferior vena cava and lungs.

CASE 25.—Pitroeffy-Szabó (1935) reported the case of a girl of 3½ years. She was normal at birth. Six months after birth her parents noticed abnormal development particularly as to the weight and length. At 1 year, her voice became deeper. At the age of 3 years, she showed an abundant growth of hair over the entire body, face and chin, with acne on the back and face. The external genitalia appeared to be normal. A roentgenogram of the skull showed a normal sella turcica. An operation was performed, and a tumor the size of child's head touching the liver was found in the upper pole of the kidney. Because of increased vascularity, removal was not attempted. A few days later the patient died. The tumor weighed 707 Gm. and was encased by a vascular capsule. The histologic picture of the tumor showed it to have the structure of a hypernephroma of the cortex. The left adrenal gland was normal, as were the ovaries.

CASE 26.—Da Roche (1939) reported the case of a girl, 2 years and 4 months old. The patient was normal at birth. Her development was precocious, with hirsutism of the body and "deformity" of the external genitals. Her voice was hoarse, and the abdomen was enlarged. Acne was present on the face.

The clitoris was rather well developed, the labia enlarged and the vagina obliterated. Pubic hair was abundant. On examination of the abdomen a large regular mass was palpated in the right upper quadrant. A roentgenogram of the abdomen showed a large shadow on the right overlapping the shadow of the right kidney. This mass also pushed the cecum and first third of the transverse colon caudally. A diagnosis of a congenital tumor of the adrenal gland with a genitoadrenal syndrome was made. An exploratory laparotomy revealed a large tumor mass closely adherent to the liver. Removal was not attempted. No biopsy was taken. The patient died suddenly in collapse two days after the operation.

CASE 27.—Gross (1940) reported the case of a boy aged 3 years who was normal at birth and developed normally until four months prior to admission to the hospital. He was of large stature, appearing like a boy of 11 years. His genitalia were larger than normal, like those of an adolescent youth. His voice was deep. Pubic and mammary hair was present. A palpable mass was noted on the left side of the abdomen, and a diagnosis of adrenal neoplasm was made. Ossification was like that of a 6 to 7 year old child. Operation was performed, hemorrhage occurred and the tumor ruptured. The patient died two hours later from shock. The mass weighed 640 Gm. Metastases were not mentioned.

CASE 28.—Albert (1941) reported the case of a girl 2 months of age who had an abdominal swelling of a few weeks' duration. She was fretful, and she was also wasted and puny. The breasts were small. Hair was present in the axillas and the pubic regions and was of male distribution. The clitoris was enlarged, with a small glans and the rudiments of a prepuce. An enormous hard ovoid mass was palpated in the right side of the abdomen. A diagnosis was made of an adrenal cortical tumor. An exploratory laparotomy through a right paramedial transperitoneal incision was made, and a tumor of the right adrenal gland was found on the kidney. It was ovoid, 22.8 cm. in height and 15.2 cm. in breadth, with invasion of the para-aortic glands. The tumor was not removed, but a gland was taken. The patient died the next day of shock. A postmortem examination was performed, and the tumor was found attached to the diaphragm and to the inferior vena cava, with involvement of the para-aortic and portal fissure glands. The left adrenal gland and both kidneys were normal. The uterus and the ovaries were small. The growth was a cellular malignant tumor with the characteristics of a carcinoma of the adrenal cortex.

CASE 29.—Taylor and Wiseman (1942) reported the case of a boy 11 months of age. He was admitted to the hospital because of a large abdomen. The patient had been ill for two months before admission. His symptoms were constipation, refusal of food and a temperature as high as 103 F. It was at this time that the enlargement of the abdomen was first noticed by the physician, though the mother stated that it was large at birth. Since the illness, the child had grown rapidly. There were no urinary symptoms and no convulsions. Physical examination revealed that the child appeared older than the age stated. No excess hair was present on the body, but the abdomen was enlarged. A globular mass which moved on respiration was palpated in the left flank. The scrotum was enlarged. The testicles were normal in structure but larger than usual. The penis was three times the usual size. The blood pressure was normal. A roentgenogram of the skull showed a normal sella turcica. A roentgenogram of the joints showed an increased density. Fluoroscopic examination by means of a barium enema showed the splenic flexure of the colon to be pushed down. The plain roentgeno-

TABLE 3.—*Analysis of Cases in*

Case No.	Author and Year	Sex	Condition at Birth	Age at First Symptoms, Yr.	Age at Death, Yr.	Size of Genitalia			Age at Appearance of First Menses, Yr.	Body Development	Breasts	Voice Change
						Clitoris, Penis, Cm.	Labia or Scrotum	Uterus, Ovaries or Testes				
32	Bevern and Romkild 1802	F	....	2¾	3½	.....	.....	.....	.....	Fat "like woman of 20"	.....	.....
33	Tilesius 1803	F	....	...	4	.....	.....	.....	.....	Very fat	Large	.....
34	Cooke 1809	F	Normal	4	7	Hypertrophied, 2.5	Precocious	Normal	None	Large skeleton, fat	Normal	Strong
35	Pitman and Ogle 1865	F	Normal	2⅜	3	Precocious	Precocious	.....	.....	Stout	.....	Rough
36	Colcott-Fox 1885	F	Normal	5/6	2	Precocious	Precocious	Large	.....	Enormous	.....	.....
37	Dickinson 1885	F	....	1	3	.....	.....	.....	.....	.....	.....	Harsh
38	Orth 1893	F	Normal	1/6	4½	Like small penis	Precocious	.....	.....	.....	.....	.....
39	Bulloch and Sequeira 1905	F	Normal	10	11	.....	.....	Large cervix; ovaries with corpora lutea	10	Looked like a woman of 40	Large	.....
40	Ritchie 1905	F	....	...	4	Precocious	Precocious	.....	None	.....	.....	.....
41	Guthrie and Emery 1907	M	Normal	2	4¾	Not duly developed	Not duly developed	.....	.....	Like "burly brewer's drayman"	.....	.....
42	Dun and Glynn 1911	F	Normal	3	5	No hypertrophy	No hypertrophy	.....	.....	Tall and fat	Normal	.....
43	Baldwin 1914	M	Underdeveloped	1½	5⅝	10.2	.....	Small	.....	Precocious	.....	Mannish
44	Tschernobrow 1919	M	....	8	11	.....	.....	Normal	.....	Like a 15 to 17 year old	.....	Low
45	Schmidt 1924	F	Normal	8	9	2	Very large	.....	8, every 4 weeks	Obese and strong	Small	Mannish
46	Browder 1927	M	....	¾	3	7.8	.....	Immature	.....	Herculean type	.....	Mannish
47	Lundh 1929	F	Normal	3	3½	3	Large	Normal	None	Obese	Not large	Coarse
48	Macera 1929	M	Normal	2 5/12	2⅝	4 7 erect	Well developed	.....	.....	Obese	.....	Hoarse
49	Moltschanoff and Davydowski 1930	F	Normal	4	6	3	Very large	Normal	None	Decided obesity	.....	.....
50	Meyer and Frumess 1931	F	....	..	13	...	.....	.....	12½	Looked 19 to 20	Slight	.....
51	Birrell 1932	F	Normal	4	5	Markedly hypertrophied	Unusually large	.....	None	Obese	Nipples pronounced	.....
52*	Rowntree and Ball 1933	M	....	1½	2½	Like adult	Like adult	.....	.....	.....	.....	Low and manly
53	Little 1936	F	Normal	3½	7½	3 by 1	Hypertrophy	Small	.....	Masculine	.....	Deep
54	Crooke and Callow 1939	F	....	6	6	Enlarged	Enlarged	.....	.....	Obese and muscular	Not large	.....

* No autopsy obtained.

Recursuties		Palpable Abdominal Mass, Side	Diagnosis	Therapy	Tumor		Histologic Observations	Metastases	Postmortem Diagnosis, Side	Outcome
Beard	General				Size, Cm.	Weight, Gm.				
+	..	..	.....	.....	Large	..	.....	.....	Tumor of left adrenal gland	
..	..	..	.....	.....	Goose egg	..	.....	Liver	Hypernephroma of left adrenal gland	
+	+	..	Hydrocephalus internus	.....	Extended from kidney to kidney	..	.....	.....	.....	Died from convulsions
+	+	Left	.....	.....	Large	955	Encephaloid	Liver and lungs	Tumor of left adrenal gland	
..	+	..	.....	.....	.....	682	Giant cell tumor	Lung	Hypernephroma of left adrenal gland	
..	..	..	.....	.....	.....	..	Encephaloid	Liver	Adrenal tumor	
+	..	Right	.....	.....	.....	..	Carcinoma	Liver and lungs	Tumor of right adrenal gland	
+	..	Left	.....	.....	.....	1,409	.....	Liver and lungs	Hypernephroma of left adrenal gland	
..	..	..	.....	.....	.....	..	Large cells	.....	Adrenal hypernephroma	Died following an osteotomy
+	..	None	.....	.....	Walnut	..	Carcinomatous and very complex	None found	Hypernephroma of left adrenal gland	Died from acute miliary tuberculosis
+	+	Right	.....	.....	19 by 12.7 by 10.1	1,250	.....	None found	Hypernephroma of right adrenal gland	Died from pneumonia
+	..	Left	Adrenal hypernephroma	.....	31.7 by 22.9	..	.....	Liver and lungs	Hypernephroma of left adrenal gland	
..	..	Abdominal swelling	Liver disease	.....	Large as a head	..	Large epithelial cells	Liver	Hypernephroma of right adrenal gland	
+	+	..	Pseudohermaphrodite; kidney abscess	.....	.....	..	Malignant tumor	Liver and lungs	Carcinoma of of right adrenal gland	Died from sepsis
+	+	Left	.....	.....	.....	..	.....	Inferior vena cava; left adrenal vein and lungs	Hypernephroma of left adrenal gland	
..	+	Left	Tumor of left adrenal gland	.....	.....	..	Exquisite malignant growth	Both lungs	Carcinoma of left adrenal gland	Died from convulsions
+	+	Right	.....	.....	20 by 12 by 14	1,450	Malignant cortical suprarenoma	Liver and lungs	Carcinoma of right adrenal group	Died from convulsions
+	+	Right	Adrenal hypernephroma	.....	5 by 5 by 6	..	Malignant adrenal struma	Breast bone	Hypernephroma of right adrenal gland	Died from miliary tuberculosis
..	..	Palpable liver	Cystic adenoma of liver	.....	13 by 17 by 7	..	.....	Liver, pleura, mediastinal and mesenteric nodes	Hypernephroma of left adrenal gland	Died from intra-abdominal hemorrhage
..	+	..	.....	.....	.....	..	.....	Left kidney and renal vein; liver	Tumor of right adrenal gland	
..	..	Right	Malignant growth	High voltage roentgen therapy	.....	..	.....	Left thigh	Carcinoma of right adrenal gland	
+	+	Not palpable	Carcinoma in left upper part of the abdomen	Awaiting operation	15 by 13 by 5	..	.....	Lung and liver	Hypernephroma of left adrenal gland	Died from convulsions and pneumonia
+	..	Left	.....	.....	28 by 27 by 14	..	Giant cell carcinoma	Left kidney liver and abdominal glands	Carcinoma of left adrenal gland	Died from acute heart failure

gram of the abdomen showed the shadow of a mass on the left side. A pyelogram was taken which showed that the kidney was displaced into the iliac fossa and was partially rotated. A preoperative diagnosis of tumor of the left adrenal gland was made. An operation was performed through an incision in the left lumbar region. A mass was found free of the kidney, with a tongue of tissue extending across the aorta and enmeshing the inferior vena cava. The child went into shock during the operation and died thirteen hours later. A postmortem examination was made. The tumor weighed 294 Gm. and was 10 by 10 by 7 cm. Microscopically it showed distinct anaplasia. A diagnosis of carcinoma of the adrenal cortex was made.

CASE 30.—De Jaeger (1942) reported the case of a girl 8 years of age. At birth her parents noticed some genital maldevelopment. At the age of 15 months a slight bloody discharge from the vagina was noticed. Her mother thought this was precocious menstruation, but the bleeding did not recur. At 18 months of age the voice changed to a deeper tone. At the age of 2 years masturbation was noticed, and subsequently development of the body and muscles was pronounced and rapid. The ossification of the carpal bones was that of a 12 year old child. Generalized hirsutism was present, with hair on the upper lip and also in the pubic region. The mammary glands were not developed. Examination of the genitalia showed a hypertrophied clitoris which looked like a small penis. The labia majora and labia minora were also hypertrophied. The vagina was normal. The uterus was small. The abdominal wall was flaccid and distended. Roengenographically, a small mass, the size of a chicken egg, appearing calcified, was present between the tenth and the twelfth rib on the right side; it moved on respiration. A diagnosis of adrenal tumor was made because of the hirsutism and the masculinization. The urine showed no increase in hormonal excretion. An operation was performed and the tumor was found adherent at its upper pole and was liberated with difficulty. The immediate postoperative condition was good. One month after the operation the patient's temperature suddenly dropped. Profuse perspiration was noted, and the child went from shock to complete collapse and died. The postmortem examination showed a carcinomatous tumor of the adrenal cortex.

CASE 31.—Kempton and Lohr (1942) reported the case of a girl of 15 months who was normal at birth. When the child was 6 months old the abdomen became enlarged, and pubic hair was noticed. Later hair was present on the face, abdomen and back. The child grew rapidly. At 15 months of age, the hair was abundant, and there was hair on the upper part of the cheeks. Her voice was heavy. The labia and the clitoris became larger. There was a fulness in the left side of the abdomen. A roentgenographic examination revealed the kidney displaced toward the midline. An operation was performed, and a carcinoma of the left adrenal gland was removed. It weighed 610 Gm. and was 13 by 10 by 7.6 cm. The patient died of shock twelve hours after the operation.

III. Cases Without Surgical Intervention.—CASE 32.—Bevern and Romkild (1802) reported the case of a girl whose first symptoms started at the age of 2¾ years and who died at the age of 3½ years. She was fat, "looking like a woman of 20." She had abundant hair on the face and pubes. A postmortem examination revealed a large tumor in the left side of the abdomen. Neither the exact attach-

ments nor the adrenal glands were mentioned. The case was apparently typical clinically, but the pathologic proof is insufficient.

CASE 33.—Tilesius (1803) reported the case of a girl aged 4 years who was excessively fat and had large mammae and well developed pubic hair. A postmortem examination revealed a tumor of the left adrenal gland the size of a goose egg, with metastases to the liver.

CASE 34.—William Cooke (1809) [2] reported the case of a girl aged 7 years who was enormously fat and had a large skeleton. Her symptoms started at the age of 4 years. There was copious hair on the face, body and genitals. She had precociously developed genitalia, with a clitoris resembling a penis nearly 1 inch (2.5 cm.) in length with its glans clearly defined. At the age of 7, she acquired acute meningitis and died in convulsions. Postmortem examination revealed internal hydrocephalus. Neither adrenal gland was found. A scrofulous abscess was present, affecting the liver and extending to the left kidney. This kidney also had a calculous concretion. A large irregular tumor was found under the right lobe of the liver, resting on but not invading the left kidney. The tumor extended from the upper pole of one kidney to the upper pole of the other. On section of this tumor a quantity of thick chocolate-colored material was pressed out. No microscopic report was made.

CASE 35.—Pitman and Ogle (1865) reported the case of a 3 year old girl who was normal at birth. Symptoms began at 2½ years. At the age of 3, she was stout and weighed 44 pounds (20 Kg.). She had a sullen expression, a rude and savage disposition, a rough voice and a voracious appetite. Her skin was "gypsy color." General hypertrichosis with heavy eyebrows, mustache and pubic hair was present, with premature development of the genitals. A tumor was palpable in the left side of the abdomen. A postmortem examination revealed a tumor of the left adrenal gland weighing 955 Gm., with secondary growths in the liver and lungs. The other organs were normal. The tumor was described as a "large mass of encephaloid cancerous growth."

CASE 36.—Colcott-Fox (1885) reported the case of a girl of 2 years who was normal at birth. She was enormous at 10 months of age and had a ravenous appetite. She was of a dull intellect. Her skin had a dusky pallor; development of the vulva, labia and clitoris was premature. The pubic and body hair was prominent. The tumor was present on the left side of the abdomen. The postmortem examination revealed that the tumor replaced the left adrenal gland and weighed 682 Gm. The uterus and the ovaries were large. There were metastases to the lungs. The tumor was described as a giant cell sarcoma (Glynn described it as a hypernephroma).

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2. This appears to be the same case as that cited by Linser (page 299) and also cited by Hoag. Their reference (Cooke, W.: Phil. Trans. Royal College of Surgeons, London, 1756) could not be verified by us after a thorough search of the bibliographic reference books. Their case of a girl, Louise Flux, aged 7, conforms completely to the facts as found in our case herein reported. Rolleston was also of our opinion but erroneously cited his reference as *Medico-Chirurgical Transactions*, 1811. The case of Louisa Flax, aged 7, appears in the *Medico-Chirurgical Transactions* (**2**:17-23, 1817). It thus appears that credit for describing the first case of adrenogenital syndrome in children belongs to Bevern and Romkild. Cooke, nevertheless, was the first to report such a case in the English literature.

CASE 37.—Dickinson (1885) reported the case of a girl of 3 years, dull of intellect and with gypsy-colored skin. She had a harsh voice and a ravenous appetite and had had hair on the pubes since the age of 1. The condition of the external genitals was recorded as large. A postmortem examination revealed a tumor of the adrenal gland (the side not recorded) with 2 metastases to the liver. The growth was described as "encephaloid." (Rolleston has stated that this is the same case reported by Pitman and Ogle previously.)

CASE 38.—Orth (1895) reported the case of a girl aged 4½ years. Her first symptoms occurred at 2 months of age. She was normal at birth. Her clitoris was like a small penis. Development of the other external genitalia was premature. She had hair on the pubes and face and she had been shaved for the past six months. The tumor was felt in the right side of the abdomen for 2½ years. A postmortem examination revealed that the mass replaced the right adrenal gland, and that there were secondary growths in the liver and lungs. This was described as a "carcinoma" (Hoag and also Glynn described it as a hypernephroma).

CASE 39.—Bulloch and Sequeira (1905) reported the case of a girl of 11 years. She was normal at birth. She was dull mentally and dark skinned with a large face, and she "looked like a stout little woman of about 40 years." Her height was 4½ feet, and she weighed 87 pounds (39.5 Kg.). Her symptoms started with menses at the age of 10, her breasts became large and she resembled a sexually mature woman. There was hair on her chin, lips, pubes and axillas. A tumor was found in the left side of the abdomen. A postmortem examination revealed that the tumor had replaced the left adrenal gland. It weighed 1,409 Gm. The thyroid and parathyroid glands were hypertrophied. Enlargement of the cervix of the uterus was noted. The ovaries were fairly large and corpora lutea were present. Secondary growths were found in the liver and lungs. This tumor was reported as a carcinomatous hypernephroma.

CASE 40.—Ritchie (1905) reported the case of a girl aged 4 years who had pubic hair was thought to be a hermaphrodite, but Professor A. Thompson expressed the opinion that the genitals were normal except for the size, resembling those of a developing woman. No menses occurred. She was well nourished. Her death followed an osteotomy. At postmortem examination an unsuspected adrenal tumor was found which was described as a "sarcoma with large cells," the kind called a hypernephroma by Glynn.

CASE 41.—Guthrie and Emery (1907) reported the case of a boy of 4¼ years. He had had hair on his face and pubes since the age of 2 years. He was normal at birth. Later he became as stout as a "burly brewer's drayman" in miniature. He weighed 43½ pounds and was fat; his eyebrows were bushy. His genitalia were "not unduly developed." He had convulsions three months before hospitalization. He died of acute miliary tuberculosis. No abdominal tumor was palpable. A postmortem examination revealed a disseminated miliary tuberculosis and a tumor of the left adrenal gland the size of a walnut. The right adrenal gland was not found. The thymus, thyroid, hypophysis, epiphysis and testicles were normal, with no spermatogenesis. No secondary growths were found. The tumor was reported as a malignant hypernephroma; it was a carcinomatous mass which was very complex.

CASE 42.—Dun and Glynn (1911) reported the case of a girl aged 5 years who was well until the age of 3 years, when she complained of abdominal pains. There was precocious development of the body. She was unusually tall, fat, and flabby, with hair on the scalp, upper lip, pubes and back. The skin was dry and harsh; acne and seborrhea were present on the face and shoulders. There

was no pigmentation. There was no hypertrophy of the clitoris or mammae and no evidence of menses. In the last six weeks of life an abdominal mass was palpated on the right side. She had convulsions and died from pneumonia. A postmortem examination revealed a tumor of the right adrenal gland weighing 1,250 Gm. and measuring 19 by 12.7 by 10.1 cm., encapsulated and free of the kidney. In the pancreas, the islets of Langerhans were prominent. The amount of colloid in the thyroid gland was a quarter of the normal amount. The ovaries, the pituitary gland and the left adrenal gland were normal. No secondary growths were found. This was reported as a malignant hypernephroma of the adrenal gland.

CASE 43.—Baldwin (1914) reported the case of a boy aged 5 years and 10 months. Sexual precocity was evident at the age of 18 months. He was underdeveloped at birth. Subsequently, there was precocious physical development. He had a voice like a man and acne on the face, chest and back. He had hair on his face which required shaving and also hair on the pubes. The genitalia were like those of an adult, the penis being 10.7 cm. in length. The testicles were in the canal but were small. An abdominal tumor was palpable on the left side, and a diagnosis of hypernephroma of the adrenal gland was made. The patient died and postmortem examination revealed the pituitary, pineal, thyroid or parathyroid glands to be normal. A hypernephroma of the left adrenal gland was found, measuring 31.7 by 22.9 cm. The kidneys were free. A hypernephroma of the right adrenal gland, the size of a walnut, was also found. Secondary growths were present in the liver and in the lungs. The testicles were normal. A diagnosis of hypernephroma of the adrenal cortex was made.

CASE 44.—Tschernobrow (1919) reported the case of a boy aged 11 years. For three years a strong growth of hair on the mons pubis and also a low voice had been evident. During the eight to nine weeks prior to examination, he had a swelling of the abdomen and pronounced ascites. Fifteen liters of fluid was withdrawn from the peritoneal cavity. It was thought that he had hepatic disease and that the ascites was due to portal thrombosis. Subsequently he was thought to have a hypernephroma. Soon he became drowsy and died. A postmortem examination revealed a tumor the size of a head located between the liver and the right kidney, flattening the latter. The tumor was separated from the kidney by its capsule. When examined microscopically the tumor was seen to consist of large epithelial cells and to look like a hypernephroma. It was diagnosed as a primary growth of the right adrenal gland bordering on a sarcoma. Metastases were present in the liver.

CASE 45.—Schmidt (1924) reported the case of a girl aged 9 years. Her birth was normal as was development until the age of 8 years, when it was noticed that she was extremely strong and could throw down boys larger than she. Vaginal bleeding was present and irregular at four week intervals. Psychic changes were also present. She often complained of dizziness, sleepiness and backaches, and she had occasional nosebleed. She soon became depressed, segregating herself from other children. Subsequently, growth of hair on the chin, pubes and axillary regions was noticed. Her voice changed, becoming mannish; her skin became dark, and she became obese and strong. Three weeks before consultation, boils developed over the patient's entire body. She also complained of pain in the abdomen, was restless and had a high fever. At times she became delirious. An examination at the hospital showed many pustules over the body and subcutaneous abscesses on the back. Hair was present on the breasts, arms, legs and pubes. A strong growth of eyebrows was present, with a bushy beard and

with hair on the upper lip. The mammary glands were small. The abdomen protruded like a ball and was sensitive to pressure. The liver was palpated in the navel region. The labia were extremely large, and the clitoris was 2 cm. in length. The vaginal introitus was deep. A clinical diagnosis of pseudohermaphroditism, furunculosis and possible abscess of the kidney was made. The patient died, and an autopsy revealed the left adrenal gland to be knotty and hyperplastic. In the right adrenal gland there was a knotty nodular tumor surrounded by a firm capsule which histologically was of a malignant type. A diagnosis of malignant tumor of the right adrenal gland with metastases to both lungs and liver, associated with hyperplasia of the left adrenal gland, was made.

CASE 46.—Gordon and Browder (1927) reported the case of a boy of 3 years. Onset of pubertas precox occurred at the age of 9 months. He was of the Herculean type, with a mannish voice, acne, pubic hair and also a mustache and hair elsewhere on the face and on the back. The external genitalia were like those of a boy of 16 years. Ossification was premature. He was dull mentally. An abdominal mass was felt on the left side. The penis was 7.8 cm. long, and the epididymis was palpable. Rectal examination revealed a smooth, firm prostate. Postmortem examination showed a carcinoma of the left adrenal gland which extended into the left adrenal vein and the inferior vena cava. Metastases to the lung were also present. The right adrenal gland was absent. The testes were immature, with no spermatogenesis. The thyroid, pancreas, pineal and pituitary glands were normal.

CASE 47.—Lundh (1929) reported the case of a girl, aged 3½ years. She was normal at birth. Development was normal until the age of 3 years, when it was noticed that she began to grow very rapidly and that she had a ravenous appetite, and had become fat. Hair was present over the pubes, buttocks and lower limbs. The labia majora were "swollen." A vaginal discharge was present, but no bleeding was noted. The abdomen was distended, and a hard tumor about the size of a man's head was palpable. No axillary hair was present. The breasts were not enlarged. The labia majora were large. The clitoris was 3 cm. in length and appeared like a little finger with a prepuce that showed hypospadic formation on its under surface. The vagina was normal. The uterus was small, and the adnexa were normal. The voice was coarse. The thyroid cartilage was developed and prominent. A roentgenogram revealed a large shadow in the left upper quadrant of the abdomen, and a pyelogram of the left side showed a downward and lateral displacement of the left kidney with a tumor shadow above. The pelvis of the kidney was of normal outline. The diagnosis was an inoperable tumor of the left adrenal gland. After violent clonic spasms and unconsciousness, the patient died. Microscopically, the brain and all the endocrine organs were normal except for a large retroperitoneal tumor in the region of the left adrenal gland. The kidney and other organs were free. No secondary growths were present in the liver. Microscopic examination of this mass showed an exquisite malignant growth, with diffuse necrosis and hemorrhage and with some calcific incrustrations. Secondary growths were present in both lungs.

CASE 48.—Macera (1929) reported the case of a boy 34 months old. His birth and subsequent development were normal. At 29 months of age enlargement of the abdomen, with hypertrichosis, was noticed. Examination showed the patient to be obese and to have hair on the trunk, face, chest and genitals. His voice was hoarse. An abdominal examination revealed a painful mass on the right side. It was solid and had a smooth surface. The penis was 4 cm. long

and 7 cm. on erection. The scrotum and testicles were well developed, the latter having a glandular consistency. A roentgenogram made after administering an enema of a bismuth preparation revealed a tumor pushing the transverse ascending and descending colon downward. The patient was admitted to the hospital, where he had convulsions and died. An autopsy revealed pulmonary and hepatic metastases. The left adrenal gland was extremely small. In the right adrenal gland examination revealed a large tumor 20 by 12 by 14 cm. in size, weighing 1,450 Gm., which was attached to the liver and easily separated from the kidney. A histologic diagnosis of malignant corticosuprarenoma was made. The testes showed azoospermia.

CASE 49.—Moltschanoff and Davydowski (1930) reported the case of a girl aged 6 years. The child was normal at birth. Her development was more rapid than normal as shown by a large body with early development of the sex organs, generalized hirsutism and extreme obesity. To about the age of 4 years, the child was normal and lively. In the fifth year, the growth was strongly accelerated, and hair then appeared on the pubes, the face and the whole body. The clitoris was enlarged. When the child was 5½ years old, she had a vague acute illness, with a high fever and delirium. This left her with a paralyzed left arm and leg. Two weeks prior to her admission to the hospital, there was a return of motion to the paralyzed muscles. At this time there was also observed a noticeable development of hair over the entire body and the face. There was also a great increase in subcutaneous fat, especially of the face and abdomen. Examination of the abdomen showed a solid abdominal mass in the right upper quadrant which was not distinguishable from the liver and moved with respiration. The external genitalia were like those of a grown woman, with greatly enlarged labia majora, hymen and vagina. The clitoris was 3 cm. in length and looked like a small male organ. The urethra opened on the under side of the clitoris. A rectal examination revealed the uterus to be thin and small. No menses occurred. Roentgen examination of the carpal bones showed seven centers of ossification instead of the normal four or five. The sella turcica was normal. The patient soon died in the hospital from a rapidly developing heart condition, complicating tuberculosis and septicemia. A clinical diagnosis of hypernephroma of the adrenal gland and also of hydrocephalus with left-sided hemiplegia was made. An operation was not performed. A postmortem examination showed the general physical appearance as described. In the peritoneum were many miliary tubercles. The uterus was normal. The ovaries contained many cysts. The spleen as well as the liver revealed many tubercles, probably of tuberculous origin. In the kidneys there were many pale soft areas with caseous centers. The left adrenal gland appeared normal. In the region of the right adrenal gland there was a growth 5 by 5 by 6 cm. in size. The main portion of this mass lay in the depths of the fissure on the under surface of the liver. Numerous tubercles were present in the lungs. Metastases were found in the breast bone. Histologically the tumor was a malignant adrenal struma.

CASE 50.—Meyer and Frumess (1931) reported the case of a girl of 13 years who complained of abdominal pain, acne and rash on the face and throat. The menses had started at the age of 12½ years. Her menses had stopped during the past three months. Her appearance was like that of a 19 or 20 year old girl. She had slight development of the breast, and copious pubic hair of male distribution. A large nodular abdominal liver was palpable, and a diagnosis of cystic adenoma of the liver was made. The patient died subsequently of an intra-abdominal hemorrhage. A postmortem examination revealed a hypernephroma of the left adrenal gland measuring 13 by 17 by 7 cm. Secondary growths were present in the

liver and the pleura and in the peritoneal and the mediastinal nodes. In the right adrenal gland there was a cortical adenoma.

CASE 51—Birrell (1932) reported the case of a girl aged 5 years. The child was normal at birth. When she was 4 years old symptoms of obesity, rapid growth and the development of general hirsutism were observed. No menses were noted. She also had acne and comedos. The pubic hirsutism was of female distribution; hair was also present on the arms and back. The blood pressure was 135 systolic and 80 diastolic. The breasts were not enlarged, but the nipples and areolas were pronounced. The labia majora were unusually large. The clitoris was noticeably hypertrophied. A roentgenogram of the pituitary fossa was normal. Clinical examination of the abdomen at this time showed no abnormal conditions. After a month, the tip of the liver and of the spleen could be palpated and a resistance deep in the right loin was present also. The child later complained of abdominal pains; her death occurred soon after. A postmortem examination revealed a large tumor invading and largely destroying the left kidney, with absence of any recognizable adrenal gland. There was invasion of the renal pelvis and of the renal vein. Secondary growths were also present in the liver. The right adrenal gland and the kidney were normal.

CASE 52.—Rowntree and Ball (1933) reported the case of a 30 month old boy who had an abdominal mass of one year's duration and a swollen left knee of one week's duration. A year previously the abdomen had been found to be full, and this symptom was followed by the growth of dark hair in the axillas and the pubic region. The penis and scrotum were as large as an adult's. The voice was low and manly. Five months previously the abdominal tumor had been palpated in the right upper quadrant, and at that time it was found to be hard and irregular. A hard swelling was also present in the left thigh, which was thought to be metastatic. An operation was inadvisable, and a diagnosis of a malignant process was made. The patient was sent home for high voltage roentgen therapy, and he died there in a few months. No postmortem examination was made.

CASE 53.—Little (1936) reported the case of a girl 7½ years old who was normal at birth. When she was 3½ years old, hirsuties was noticed on the body, face, chin, upper lip and pubes. Her voice was deep. Acne was present on the face. Her eyebrows were heavy, and she had a masculine build. Her blood pressure was 120 systolic and 80 diastolic. She had hypertrophied external genitals, and the clitoris was 3 cm. long and 1 cm. thick. The uterus was small. A pyelogram showed a distortion of the pelvis and the calices of the left kidney. A diagnosis of a carcinomatous mass in the upper left quadrant of the abdomen was made. The child was fat. There was muscular weakness, and subsequently convulsions occurred, followed by pneumonia and by death. During life the mass was not palpable. Postmortem examination revealed a carcinoma of the left adrenal gland 15 by 13 by 5 cm., which was encapsulated. There were secondary growths in the lung and liver. The pituitary gland was normal, both microscopically and grossly. The thyroid and parathyroid, thymus and pineal glands were also normal. The right adrenal gland was atrophic. Operation was contemplated, but the patient died two days before the operation.

CASE 54.—Crooke and Callow (1939) reported the case of a girl of 6 years (case 2 of their series). She was examined in July 1936, and a swelling of the abdomen of two weeks' duration was noted. Pubic hair had been present for one month. She had nocturnal enuresis. The patient was well developed and healthy looking. The breasts were not enlarged, and no hair was present on the face or axillas. No striae were present. Blood pressure was 150 systolic and 120 diastolic. Examination of the abdomen showed a hard, large mass in the left loin.

Albuminuria was present. The sugar tolerance was normal. In November 1936 the patient was admitted to the hospital. She was now obese, her face was coarse with acne, and hair was present on the upper lip. She also was more muscular, and the hair was more generalized. The clitoris and labia majora were enlarged. There was no osteoporosis. The bony epiphyses were normal. Ascites soon developed and the patient died of acute heart failure. A postmortum examination revealed a tumor of the left adrenal gland, 28 by 27 by 14 cm., invading the adjacent surface of the kidney. Glands in the lumbar region, the celiac glands and a gland in the posterior mediastinum were involved, as well as the liver. Histologically it was a polygonal, polymorphic, and frequently mononucleated or multinucleated giant cell carcinoma of the adrenal cortex. No tumor was present in the anterior lobe of the pituitary gland, but some hyaline changes were present in many basophil cells.

CLASSIFICATION OF ADRENAL CORTICAL NEOPLASMS

The first extensive classification of adrenal tumors manifesting cortical hyperactivity is that of Apert (1910) who described 5 types of "hyperepinephry," as follows:

1. Of the embryonal period, resulting in the hermaphrodite with internal female genital forms and external male genital forms, undeveloped breasts, a hypospadic clitoris and a vulval cul-de-sac.
2. Of the fetal period, when hirsuties is evident, with enlargement of the clitoris. The uterus and the ovaries are atrophied.
3. Of the prepuberty period, leading to abnormal body development, with puberty precox, adipositas, hypertrichosis and hypertrophy of the clitoris.
4. Of maturity. Adiposity and hypertrichosis are present, and the menses stop.
5. Near and after the menopause, resulting in adiposity, hypertrichosis and genital dysfunction, for example menorrhagia (but the clinical picture is indistinct).

Cortical tumors also caught the fancy of Gallais (1912), and he mustered his observations to bring his classification into four types, as follows:

1. Congenital.
2. Early acquired.
3. Menstrual.
4. Obstetric.

Hoskins was more concise than Gallais, and in Abt's "Pediatrics" he classified adrenal cortical virilism into three types.

1. Hypertrophy during fetal life, producing pseudohermaphroditism.
2. Hypertrophy during postnatal life, producing pubertas precox.
3. Hypertrophy after puberty, producing virilism or hirsutism.

More recently Cahill, Melicow and Darby have classified adrenal cortical neoplasms according to their own clinical observations—the basis being age, sex and amount, as well as kind, of hormone secreted.

Their classification is as follows:

1. No recognizable hormonal changes.

2. Changes due to excess androgens: (*a*) in a girl tending toward adult masculinity, (*b*) in a woman toward masculinity, (*c*) in a boy toward adult masculinity.

3. Changes due to excess estrogen: in a man tending toward femininity.

4. Changes due to excess androgens and other steroids: Cushing's syndrome with associated sexual changes (mostly in females).

5. Changes due to excess of other steroids related to metabolism: Cushing's syndrome without sexual changes in male and female.

In this paper we are concerned only with the clinical syndrome of 2 (*a*) and (*c*) of Cahill, Melicow and Darby. The paper is further limited to the consideration of only the malignant cortical neoplasms producing these clinical pictures.

In addition this paper does not intend to deal with Marchand tumors, which are neoplasms of adrenal rests. Such rests have been known since Morgagni and have been found in the kidney between the renal and solar plexuses, under the capsule of the liver, around the pancreas, along the course of the spermatic vein, in the epididymis, in the hilus of the ovary and testes, in the rete of undescended testis and in the leaves of the broad ligament.

ETIOLOGY

It would be interesting at this point to bring out the theories put forward by some of the original authors on this subject to account for the secondary sex manifestations. Adrenal hyperactivity is said to be the cause in at least 15 per cent of female pseudohermaphrodites and in 0.7 per cent of male pseudohermaphrodites (Glynn). It was strongly suggested in the work of Ivy and Green that in infants who have no adrenal hypertrophy or tumor the condition may be the result of the effect of abnormal hormonal activity of the mother on the fetus during gestation.

Four theories have been discussed:

1. That of Bulloch and Sequeira (1905) and of Glynn (1912), who expressed the opinion that the effect is due to an accentuation of the normal physiologic function of that portion of the organ—the cortex.

2. That of Gallais (1905), who stated that the effect is the result of pluriglandular disturbance, with hyperfunction of the cortex affecting the ovary in the female.

3. That of Blanchard (1916), who said that the effect is due to disturbances of the sex glands.

4. That of Krabbe (1921), who postulated that the effect is due to the development of the tumor from sex glands of the male type, which early in the embryo become involved in adrenal cortical tissue.

Apparently, among these postulations, that of Bulloch and Sequeira and of Glynn bears up best under the recent impounding of a vast hormonal research activity.

It would be fruitful at this time to bring out some of the salient features of the hormonal activities set up by these overactive adrenal glands.

The adrenal cortex elaborates hormonal substances, sterol lipids chemically, some of which are necessary for the maintenance of life. At least two distinct types of hormones are produced. One type has its effects on the metabolism of salt and water, the electrolyte balance, the permeability of the capillaries, the regulation of the carbohydrate, fat and protein metabolism, the renal function, the capacity for muscular response and the resistance to stress. The maintenance of life is probably due to a combination of the various activities of the hormones of this type.

One identifiable steroid, desoxycorticosterone, has seemed to be most effective in the regulation of the salt and water metabolism, the electrolyte balance and the capillary permeability and in the preservation of renal function (Cahill). It is the excess production of this factor that produces the Cushing syndrome associated with cortical neoplasms.

The other type of hormone exhibits the action of the male hormone. It is a beta ketosteroid (dehydroisoandrosterone) and differs slightly from the testicular male hormone, androsterone, which is an alpha-ketosteroid. The female hormones estrone and progesterone are also secreted by the adrenal glands. Combinations of this type of excessive hormonal activity give rise to virilism in the infant girl and the woman, to virilism in the infant boy and to femininity in the man. These hormones appear to originate in the zona reticulosa of the adrenal gland. Grollman further stated that the androgens arise particularly from the inside cells of the inner layer, and he described this as an "androgenic" layer from its suggested function. In neoplasms with excessive androgenic activity, the reticular layer of the adrenal glands shows an increase in fuchsinophile-staining granules (Broster and Vines).

In cortical tumors the dysfunction lies entirely in the adrenal tissues, and one is led to expect that "Removal of the tumor produces a symptomatic cure of the endocrine symptoms but has no effect on the anatomical changes in the pseudohermaphrodite" (Cahill).

DIAGNOSIS

In the diagnosis of adrenal tumor the physician is greatly helped by the determination of the 17-ketosteroids in the urine. In adrenal cortical neoplasms with virilism, these androgenic substances are found in large quantities in the urine. In Gross's case of a girl 3 years old, the excretion level in a twenty-four hour urine specimen rose as high as 300

international units. This then fell to a normal value (which should not be over 8 to 10 units at this age) within ten days after removal of the encapsulated adrenal neoplasm. Crooke and Callow have utilized the determination of urinary androgens in differentiating Cushing's disease (basophil adenoma of the pituitary gland) from Cushing's syndrome in tumors of the adrenal cortex (the suggested nomenclature of Kessel). These authors examined 4 patients with Cushing's syndrome, 2 of whom had basophil adenomas and 2 adrenal cortical tumors. The urinary androgens of the former were excreted in normal amounts, while the patients with cortical neoplasms excreted large quantities of androgenic material in the urine.

Large amounts of estrogenic substances have also been found in the urine, as was first discovered by Kurzrok in 1930 in a patient reported on by Cahill and his associates. The result of the Aschheim-Zondek test for pregnancy was negative. Five days after removal of the tumor there was absence of estrogen from the urine. In 1934 Frank found large quantities of estrogen in 4 patients who had adrenal cortical carcinomas; from this observation he concluded that "adrenal cortical carcinomas alone of adrenal tumors increase the amount of estrogenic substances in the urine to as high as from 1,000 to 10,000 mouse units per liter with a negative pregnancy test." In short, the finding of a large amount of urinary estrogen in the absence of a positive finding in a test for pregnancy is highly suggestive of a cortical adrenal neoplasm, but negative results do not rule out such a neoplasm. On this delightfully simple means of confirming the presence of malignant neoplasia of a visceral organ without surgical intervention, Kenyon has thrown cold water, having expressed the opinion that "Frank's experience is frankly paradoxical and seems to be an infrequent finding."

Pyelograms, intravenous or retrograde, are most revealing in attempts to localize and to determine the site of the neoplasm. Further roentgenographic localization may be attempted by a procedure introduced by Carelli and popularized by Cahill. Here, injection of air into the perirenal fascial spaces is utilized in further delineation of the adrenal glands. Instances of collapse after perirenal insufflation have been reported by Hyman and Wilhelm, but the procedure seems to be reasonably safe in the hands of the experienced surgeon. It may disclose a small tumor missed by other diagnostic procedures. However, a negative result does not exclude a neoplasm of the adrenal gland.

If a mass is palpable, a puncture biopsy can be performed as in the case reported in this paper, and a pathologic diagnosis can be made. When the surgeon is in doubt, an exploratory laparotomy is frequently profitable.

DIFFERENTIAL DIAGNOSIS

There are other pathologic conditions that one must consider before coming to a final diagnosis of adrenal cortical neoplasm because of evident sexual and somatic precocity. In the young boy, one must consider and eliminate: (1) pineal tumors, (2) midbrain and hypothalamic tumors, (3) inflammation of the midbrain and (4) testicular tumors (Gross). Pineal tumors give the classical picture of Pellizzi's syndrome. The patients are always boys and one observes pubertas precox associated with a varying degree of intracranial pressure. Over 90 per cent of the patients exhibit bilateral choking of the disk, and often there are failing vision and weakness of the internal or external rectus muscles. In lesions involving the floor of the third ventricle, the signs of an expanding intracranial lesion is minimal, but the genital hypertrophy is in the nature of a precocious maturation of the genitalia, with erections, emissions and spermatozoal production (and in the female the onset of the menstrual flow) associated with the appearance of secondary sex characteristics, excessive body development and advanced epiphysial development and fusion. Testicular tumors of the interstitial variety are extremely rare in boys and produce precocious maturation of the genital and somatic tissues. In the presence of both adrenal and gonadal tumors estrogens are found in the urine, but one gets a positive reaction to the Friedman test with testicular tumors and a negative reaction with adrenal cortical neoplasms. The obvious situation of the tumor in these cases also aids considerably, though, in arriving at a satisfactory diagnosis.

The differential diagnosis of sexual precocity in the young girl is relatively simple and entails the elimination of tumors of the floor of the third ventricle (as in boys) and of the arrhenoblastoma and granulosa cell tumor of the ovary. In the former, one finds early genital maturation, with early onset of menstrual flow associated with enormous development of the breasts, exceeding that seen in any other form of endocrinologic disturbance in childhood. The rest of the syndrome is as in the male. The arrhenoblastoma of the ovary gives rise to masculinization in the female, with hypertrophy of the clitoris and hirsutism, but this neoplasm has never been reported in girls under the age of 15. In girls with the granulosa cell tumor of the ovary genital maturation is early, as evidenced by early menarche (for example, ages 1 to 5) and the adult type of internal genitals. But the most obvious differential point is that enlargement of the clitoris does not occur in this condition.

PATHOLOGY AND METASTASIS

Pathologically the adrenogenital syndrome is not common. According to Cahill, Feinblatt and Geschickter, adrenal tumors are rare and carcinomas rarer, but when present they can usually be identified by their clinical manifestations, which affect the secondary sex characteris-

tics of the patient. The adenomas are soft, encapsulated red tumors. The carcinomas, as elsewhere, show invasive qualities, penetrating the blood vessels and capsule. Feinblatt and Alpert in reviewing 34 cases of adrenal tumors, benign and malignant, stated that "Nearly every organ in the body would be included in the list of the locations of these secondary deposits." Nevertheless, Glynn has expressed the opinion that these tumors usually increase much more slowly than most other malignant growths. Hoag similarly stated that secondary growths are late, and the "opposite gland is almost uniformly normal."

Frew has given the course of metastasis as follows: The left adrenal gland: "Secondary deposits occur in the liver, ribs and cranial bones and in the thoracic duct and certain of its tributaries" (like Hutchinson's medullary tumors). The right adrenal gland: "Secondary deposits are found on the upper surface of the liver in both lungs and in a few cases, in the cranial bones and also in the right lymphatic trunk and certain of its tributaries" (like the Pepper type of medullary tumor).

TREATMENT

The "successful removal of adrenal cortical neoplasms has been followed by results which are among the most spectacular in medicine" (Kepler and Keating).

The operative approaches for the removal of adrenal neoplasms are threefold:

1. Extraperitoneal (through the lumbar region).
2. Transthoracic (through the diaphragm).
3. Transperitoneal (through the anterior abdominal wall).

For an exploratory procedure the transperitoneal approach is best. Cahill used an anterior oblique incision, which gave him adequate exposure, and he explored the entire abdomen. The vessels are easily ligated before handling the tumor, and he recommended ligation especially in dealing with carcinomas. Better control of any operative incident is assured. Broster and Vines did preliminary transperitoneal laparotomy and explored both adrenal glands, and they followed this with their transthoracic approach. They considered this the easiest approach, as the adrenal vessels permit a slight upward movement. Nevertheless, the disadvantage of a frequent pneumothorax must be considered. Walters and Kepler did bilateral exposures to determine the presence of an opposite adrenal gland and for the localization of the diseased gland. They preferred a retroperitoneal posterolumbar incision. Young had a special retractor for thoracic procedures and used it for bilateral exposure. Young and also Hinman used incisions in the right and left lumbar regions in bilateral resections.

The postoperative treatment following adrenalectomy depends much on the type of symptoms and on the condition of the patient.

Postoperative shock due to acute adrenal deficiency is frequent. According to Cecil, 39 per cent of patients died of this shock. Sixty-five per cent had severe shock, from which only 27 per cent of all patients operated on recovered. The other 33 per cent apparently had no shock. Cahill stated that "acute adrenal deficiency is rare or does not occur in the non-hormonal adrenal cortical tumor cases, nor does it occur in those with only sex hormonal changes and that those with marked androtropic symptoms are good operative risks." Those patients who show metabolic changes (that is, who have excess hormonal action on many metabolic factors, the electrolyte, the water and salt balance and the capillary permeability, in short, those with the symptoms seen in Cushing's syndrome in children or adults) are bad operative risks. This opinion was also expressed by Thompson and Eisenhardt.

Apparently these hormonal deficiencies result from the prolonged presence in the body of an excessive secretion of adrenal hormone. Experimentally it has been shown by Ingle and Kendall that excessive injections of adrenal cortex extract can cause atrophy of the adrenal glands. Cecil has observed that in 30 per cent of the adrenal glands opposite the site of the tumor the gland "atrophies and is not congenitally absent."

The atrophy of the adrenal glands may result from inhibition of pituitary adrenotropic secretion, since adrenotropins will prevent this adrenal inhibition. Conversely, Bauer expressed the opinion that it is this excessive activity of the pituitary gland causing adrenal cortical hyperplasia (or a primary cortical neoplasia or hypertrophy) that causes the symptoms of Cushing's syndrome in basophilic adenoma. This observation has many clinical and experimental supporters. On this basis it has been suggested by Ingle and Kendall that a preoperative course of pituitary adrenotropins be given to build up and activate the remaining undiseased adrenal gland. Cahill stated that the administration of adrenal cortex extract does not change the course of a rapidly fatal collapse.

The most important treatment is that used in the acute crisis of Addison's disease. This should be anticipated by the administration preoperatively and postoperatively of potent adrenal cortex extract in adequate doses. Cahill, Walters and Kepler have further suggested the administration of adequate amounts of sodium chloride and sodium citrate and of a low potassium diet. A noticeably diminished blood volume should be treated with postoperative transfusion. After the crisis is over, the remaining gland will regain its capacity to fill the hormonal needs of the body. This "tide-over" time is indeterminate, and blood pressure and electrolyte balance should reach normal before the administration of adrenal cortex extract is discontinued.

SUMMARY OF THE FIFTY-FOUR REPORTED CASES

It would be convenient at this point to emphasize the main features of the 54 reported cases summarized in this paper. The salient facts are itemized as follows:

1. Eight patients with adrenal carcinomas have been successfully operated on.

2. The longest a patient has lived following an operation is nineteen years, and she was still alive and well the last time seen (1946).

3. Seven adrenalectomies for carcinoma were performed; all of the patients died before any was successfully operated on. The first successful operation was reported by Collett in 1924.

4. The first attempt at operative cure was made by Dobbertin in 1900. The kidney and adrenal gland were removed.

5. Babcock performed the first adrenalectomy without nephrectomy for carcinoma of the adrenal gland in 1914.

6. Thirty-one patients were operated on, only 6 of whom were males. All the males who had been operated on died.

7. The first case of a supposed carcinoma of the adrenal gland with the adrenogenital syndrome was reported by Bevern and Romkild in 1802. No histologically proved case was reported until Pitman and Ogle reported theirs in 1865.

8. The first male patient was operated on by Linser in 1903.

9. Thirty-one patients with adrenal carcinoma were operated on, of whom 23 had adrenalectomy and 8 had an exploratory laparotomy. Only 26 per cent survived the operation, and those patients successfully operated on were given surgical intervention in the last two decades.

10. The youngest patient operated on was 8 months old—the patient whose case is reported here. Apparently this patient has fully recovered.

11. In the 31 surgical cases, the clitoris (or penis) was reported as hypertrophied in 27, in 2 it was described as normal and in 2 no mention of it was made. Of the 23 nonsurgical cases, the clitoris (or penis) was noted as hypertrophied in 15, no mention of it was made in 6, and in 2 it was reported within normal limits.

12. In the 2 cases in which the clitoris was reported as being of normal size, the picture fits more closely the description of Cushing's syndrome with adrenal cortical carcinoma than that of the adrenogenital syndrome, because of the normal genitals and the obesity.

13. In all the surgical cases in which the labia or scrotum was mentioned, it was considered hypertrophied or enlarged. Only 14 reports of surgical cases describe the labia or scrotum.

14. In 2 cases the patients, both 8 years of age, have experienced vaginal bleeding. In all the other cases there was no vaginal bleeding either mentioned or by implication.

15. In 36 of the 54 reported cases changes in the voice were mentioned; in all of these cases the patient's voice was described as deep or heavy except in that reported by us in which no change was noted.

16. Of the 54 cases, in all but 3 there was pubic hair and in 2 of these 3 there was hirsutism in other areas.

17. Twenty-one of the 31 patients operated on had a palpable abdominal mass.

18. Twelve of the 23 patients not treated surgically also had a palpable abdominal mass.

19. Of the 8 cases in which there was a successful operation, a preoperative diagnosis was made in all but 1. In only 13 of the remaining 23 surgical cases was a correct preoperative diagnosis made. Of the 23 nonsurgical cases, in only 3 was a diagnosis made prior to autopsy.

20. Of the 31 surgical cases, tumors were successfully removed in 8.

21. The largest neoplasm removed weighed 2,000 Gm. the largest successfully removed weighed 1,500 Gm. and the smallest tumor removed weighed 10 Gm, In the latter case the condition was diagnosed preoperatively, and the tumor was successfully removed.

22. Microscopic studies were reported in 29 cases.

23. Of the 31 surgical cases metastases were noted in 12. No mention of metastases was made in 11, and in 7 cases no metastases could be found, though in 1 case in which there was a successful operation the tumor projected into the adrenal vein. Of the 23 nonsurgical cases metastases were described in 18.

24. Metastases were reported most frequently in the liver (19 times) and in the lungs (17 times). Metastases into the vena cava were found in 6 cases. Metastases were also found in other organs, but less frequently.

25. For some unexplainable reason the majority of adrenal carcinomas are on the left side. In 20 cases the growth was on the right side, in 31 cases it was on the left side, and in 3 no mention was made of the side involved.

26. Of the 31 surgical cases reported, the tumor in 12 was on the right side and in 12 on the left.

27. Right-sided adrenalectomy is technically more difficult because of the shorter pedicle and because the gland lies very close to the inferior vena cava. Nevertheless in our cases and in 2 others the tumors were on the right side and were successfully operated on.

28. In 26 surgical cases the patients survived the operation. The patient reported as having lived longest survived nineteen years (1946).

29. Of the case reports in which successful operations were noted, 1 patient is known to have died ten months after the operation and 1 a year later during a tonsillectomy. No current information was obtain-

able in 1 case. In 5 cases the patients were still thought to be alive, 1 nineteen years later, 1 eight years later, 1 six years later, 1 five years later and our patient twenty months later.

30. The case of William Cooke supposedly reported in 1756 appears to be the same case as that reported by William Cooke in 1817. This is the first case of adrenal carcinoma of children reported in the English literature.

CONCLUSIONS

An additional case of adrenal carcinoma with the classic adrenogenital syndrome, reported in this paper, is the eighth case to be reported in the world's literature in which there was a successful operation on a child for adrenal carcinoma.

The present case is the only one on record in which a successful operation for adrenal carcinoma has been performed on so young a child.

This is the first case in which biopsy of the adrenal glands was utilized to substantiate a pathologic diagnosis, a procedure which led to early surgical intervention and cure. This procedure is therefore recommended.

Those patients who manifest abnormal androgenic activity have a great chance of survival.

Those patients who manifest abnormal metabolic hormonal activity have a lesser chance of survival, and their course usually terminates with a manifestation of adrenal insufficiency.

An approach to the adrenal gland through the lumbar region proved satisfactory in this case.

The cases in which there was successful surgical intervention have been brought up to date, the patient in the second of such cases being (to the best of our knowledge) still alive and well at the age of 21, nineteen years after the removal of a 1,500 Gm. neoplasm.

The world's literature has been searched for cases of adrenal carcinoma in which there was the adrenogenital syndrome and 54 cases have been found including our report of an additional case.

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Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

THE EFFECT OF TRIETHYLENE GLYCOL VAPOR ON AIR-BORNE BETA HEMOLYTIC STREPTOCOCCI IN HOSPITAL WARDS. I. MORTON HAMBURGER JR., THEODORE T. PUCK and O. H. ROBERTSON, J. Infect. Dis. **76**:215 (May-June) 1945.

1. In five separate studies, triethylene glycol vapor was introduced into the air of hospital wards where patients in various stages of scarlet fever were housed. The vapor reduced the number of air-borne beta hemolytic streptococci recoverable with atomizer samplers by 65, 100, 38, 80 and 95 per cent, respectively. Reductions recorded by settling plates were smaller in magnitude.

2. In 2 wards for German measles, streptococcic cross infections ceased following the introduction of triethylene glycol vapor. However, control data which might have indicated how many more such infections could have been expected were not available. A concomitant reduction of 60 per cent in the numbers of air-borne hemolytic streptococci was produced by the glycol vapor.

3. Determination of the total numbers of bacteria in the air of the wards studied showed a diminution of 32 to 75 per cent during the periods of glycolization.

4. The results of this study together with theoretic considerations concerning the nature of bacterial particles occurring in the air of such environments, indicate that maximum effectiveness of glycol vapors in suppressing air-borne pathogenic bacteria in hospital wards probably requires the accompanying action of measures to control dust and lint.

TOOMEY, Cleveland.

Metabolism; Infant Feeding; Milk and Other Foods

FURTHER RECORDS OF THE SELF-DEMAND SCHEDULE INFANT FEEDING. FRANCES P. SIMSARIAN and P. A. MCLENDON, J. Pediat. **27**:109 (Aug.) 1945.

A similar report to this was made by the writers in 1942 (Sinsarian, Frances P. and McLendon, P. A.: Feeding Behavior of an Infant During the First Twelve Weeks of Life on a Self-Demand Schedule, *J. Pediat.* **20**:93 [Jan.] 1942). In both instances records were kept from the first day of life. Both infants were nursed from the first day, and the diet was supplemented by water only. Both were kept in the room with the mother during hospitalization—a program considered ideal by both the mother and the pediatrician.

Feeding intervals were determined entirely by the demand of the infant—when he indicated hunger by crying or "mouthing." From nine to twelve feedings were demanded per day during the first few days of life, the number gradually being reduced to five during the six and seven weeks. Behavior during feeding is described. Sleep was quiet and followed the usual irregular pattern of the newborn.

The self-demand feeding schedule and the hospitalization of mother and infant in the same room are deemed ideal for maternal adjustment. The mother is thus able to watch the early conscious moments of the infant and to learn to evaluate his wants. The close relationship stimulates the desire for breast feeding. She assumes certain responsibilities which are more easily acquired in the beginning. She learns confidence in her judgment and ability while under nursing supervision. The infant responds to contact with the mother by placid nursing behavior when unhurried by a clock-determined regimen. This early companionship of mother and infant will foster later understanding and adjustments to problems of management. Psychic birth begins when somatic birth ends.

AUTHORS' ABSTRACT.

EDEMA WITH HYPOPROTEINEMIA DUE TO A CONGENITAL DEFECT IN PROTEIN FORMATION: CASE REPORT. BELA SCHICK and J. W. GREENBAUM, J. Pediat. **27**:241 (Sept.) 1945.

This case report deals with a girl of 12 years of age who had shown edema in different parts of the body since birth. Frequently intensive swelling of the legs appeared, and fluid in the abdomen was also observed. During rest in bed the edema became less. The urine has always been free of albumin. No nephritic symptoms have been present. The general health of the child has always been excellent. She has never missed school on account of colds or sore throats.

After a long period of observation the authors were able to convince the parents that hospitalization would be necessary in order to establish the diagnosis. An intensive study of the patient showed slight symptoms of hepatic damage and a low protein content of the serum (3.3 Gm. of albumin and 0.8 Gm. of globulin per hundred cubic centimeters [4.1 Gm. of total protein]). An interesting finding, which differs from nephrosis, was that the deficit of protein content was mainly in the globulin fraction and, surprisingly, in the gamma globulin fraction. As the latter is considered to be the carrier of antibodies, it was remarkable that the general health and immunity of the child were particularly good.

The authors discuss the problem of immunity. The gamma globulin may be the carrier of humoral immunity, whereas even in case of a low gamma globulin fraction the cellular immunity may guarantee immunity. The abnormality of the hypoproteinemia may be due to a congenital defect in protein formation in the liver.

In another case published by McQuarrie and co-workers a congenital partial atrophy of the liver was found at autopsy.

AUTHORS' ABSTRACT.

THE RESULTS OF PROVIDING A LIBERALLY ADEQUATE DIET TO CHILDREN IN AN INSTITUTION: II. GROWTH IN WEIGHT AND HEIGHT. RUTH BLAIR, LYDIA J. ROBERTS and MARJORIE GREIDEER, J. Pediat. **27**:410 (Nov.) 1945.

The growth in weight and height of 151 children in an institution was followed throughout a year during which the diets were supplemented with all foods necessary to bring them up to the usual recommended dietary pattern. Comparisons were made of the rates of gain before, during and after supplementation and also between the gains of the children present in the institution throughout and those of children present irregularly or for shorter periods. The beneficial effects were shown by the following data:

1. In the preperiod the group as a whole averaged 61 per cent of its expected gain in weight; in the supplementary period the percentage rose to 140 and gains continued at a high level in the after-period. The gains for height followed a similar pattern.

2. The percentage of children under average weight for their height decreased, and there was a definite shift of the group toward more favorable weight to height status.

3. By every basis of comparison the group which was present throughout and had the benefits of the improved diet for the year fared significantly better than those present irregularly or for shorter periods.

It seems justifiable to conclude that the supplementary foods supplied some one or more dietary factors that were not present in the diet of the institution in optimal amounts. Until the requirements for the various essentials are better known, the desirability of providing the basic foods in amounts approximating those in the commonly recommended dietary pattern is indicated.

AUTHORS' ABSTRACT.

PLASMA PROTEINS AND EDEMA. J. MUNK, Maandschr. v. kindergeneesk. **10**:210 (Feb.) 1941.

Several determinations of the plasma proteins in some cases of edema (nephrotic and resulting from hunger and other causes) made according to the clinical course of the patients lead to the conclusion that neither the low albumin content alone nor the abnormal albumin-globulin ratio is the cause of the edema,, but that there is a combination of factors which promotes its occurrence.

VAN CREVELD, Amsterdam, Netherlands.

Hygiene; Growth and Nutrition; Public Health

GROWTH CHARTS FOR USE IN PEDIATRIC PRACTICE. ROBERT L. JACKSON and HELEN G. KELLY, J. Pediat. **27**:215 (Sept.) 1945.

It is an accepted practice in pediatrics to obtain measurements of height and weight as a part of the routine physical examination. If these figures are accurate and obtained over a period of time for a given child, his pattern of growth under a given regimen of living will become known. One will also have a fair index to the build of the child one is observing. To expedite evaluation it is helpful for the experienced and necessary for the inexperienced observer to have a graph showing the norms of growth for infants and children. We felt that it should be possible to devise a simple, yet reasonably complete graph that could be easily understood by the physician, medical student and nurse and meaningful even to the non-professional person.

Height-age and weight-age charts for boys and for girls have been constructed. The data on which these charts are based are 13,500 height and 11,100 weight observations of Iowa City boys and girls who were enrolled in the University well infant laboratory, preschool laboratories, elementary school and high school between 1920 and 1940. A chart is given for each sex and for each of three age groupings, the infants (0 to 12 months); the preschool (0 to 6 years) and the school child (5 to 18 years). The age ranges of these charts were established by trial and error in the pediatric clinic.

On each chart there is a set of three curves for height and for weight. The middle curve gives the average for a given age and the outside curves the values for the eighty-fourth and sixteenth percentiles. (These values correspond to points 1 standard deviation above and below the average of a normal distribution.)

Nine cases, taken from the files of the department of pediatrics and the Iowa Child Welfare Research Station, have been selected to illustrate some specific uses and interpretations of the growth charts. They reveal how closely related health and illness are to the growth of the child.

A method for estimating the build of a child under observation has been developed in terms of the relative position of the child's height and weight curves to the curves of the growth chart.

In comparing the Iowa norms with growth charts from other sources, it was found that they were as high as those of the other sources or higher. The Iowa norms are considered good for pediatric practice because they represent a relatively high level of growth.

AUTHORS' ABSTRACT.

AN EXPERIMENT IN SPEECH EDUCATION IN THE ELEMENTARY SCHOOLS. ROBERT R. PARSONS, Quart. J. Speech **31**:216 1945.

The author has made a study of education of teachers in service, in the elementary schools of West Orange, N. J. Twenty-two teachers, some having had training in the field, were given a course in speech education, a demonstration of clinical work with children having speech defects and a demonstration of speech activities in the classroom for 11 school months. The author states that the experiment demonstrates the practicability of educating teachers in service for corrective work in speech, but that regular assistance must be given to teachers over a longer period than was possible.

PALMER, Wichita, Kan.

AN INVESTIGATION OF INFANT MORTALITY AND ITS CAUSE IN CHENGTU. CHENG MEI YU, Chinese M. J. **62**:47 (Jan.-March) 1944.

During the recent years of the war an investigation of infant mortality and its causes has been made in Chengtu. The mortality rate was 126.5 deaths per thousand infants. The neonatal rate was 51.4 (40.7 per cent of the total deaths). Infant mortality was affected by the age of the baby and by the time of year, but apparently not by the parity of the mother and the month of birth. The absence of any natal care and the type of obstetric service and of infant feeding show a great influence on infant mortality. In the survey the workers planned to utilize all promising methods to reduce infant mortality.

NEFF, Kansas City, Mo.

Prematurity and Congenital Deformities

PLASTIC REPAIR OF HEREDITARY AND DEVELOPMENTAL ANOMALIES. A. P. SELTZER, Arch. Pediat. **62**:248 (June) 1945.

The author gives a general discussion of factors which have to do with the causation of congenital anomalies. The paper does not lend itself to abstracting.

GRULEE, JR., Minneapolis.

THE EFFECT ON THE FETUS OF DISEASES OF THE MOTHER DURING PREGNANCY. CHRISTOPHER BULL, Arch. Pediat. **62**:289 (July) 1945.

The author reviews the published opinions concerning the incidence of miscarriage, abortion, stillbirth and congenital anomalies or disease in viable infants born to mothers suffering from various diseases.

GRULEE, JR., Minneapolis.

THE OPTIMAL ENERGY QUOTIENT IN NOURISHMENT OF PREMATURES. MAX GRUBER, Ann. pædiat. **160**:240 (May-June) 1943.

The favorable effect on the development of the prematurely born of a method of nourishment rich in calories, emphasized by the majority of authors, is confirmed from a wide review of material. As recently advocated, the increased use and administration of colostral milk over a lengthy period definitely accelerates increase of weight, especially in the prematurely born of the lowest weight groups. An energy quotient of 115 to 125 proved optimal in most cases.

AUTHOR'S ABSTRACT.

ARTHROGRYPOSIS MULTIPLEX CONGENITA. N. I. HEYBROEK, Maandschr. v. kindergeneesk. **10**:267 (April) 1941.

The article gives a description with illustrations of 2 cases of arthrogryposis multiplex congenita observed immediately after birth and for some years. The author discusses the hypotheses mentioned in the literature. He quotes the researches of Fraser Roberts about a hereditary congenital muscle contracture in sheep, a disease resembling the human malformation and he raises the question of recessive heredity in the human condition. The author suggests that the blebs of Bonnevie in an early fetal period may be the cause of this malformation.

VAN CREVELD, Amsterdam, Netherlands.

Newborn

HEMOLYTIC DISEASE OF THE NEWBORN (ERYTHROBLASTOSIS FETALIS): CLINICAL ANALYSIS OF 55 CASES WITH SPECIAL REFERENCE TO PATHOGENESIS; PROGNOSIS AND THERAPY. MARTHA F. LEONARD, J. Pediat. **27**:249 (Sept.) 1945.

This is a review of the cases of 55 patients with hemolytic disease of the newborn treated by members of the pediatric service of the New York Hospital

from 1938 to 1944. The infants showed the typical signs: jaundice, progressive anemia, hepatosplenomegaly, edema, hemorrhage and erythroblastemia. For 84 per cent of the 33 infants tested there was the typical Rh pattern—the father and baby had Rh-positive blood and the mother Rh-negative blood; the other 16 per cent had mothers also with Rh-positive blood. Two multiple pregnancies were included as well as 2 infants of a diabetic mother, in whom the typical picture, including Rh factors, was present. Clinical signs varied greatly in degree. There was no correlation between the severity of the anemia and the degree of jaundice or the number of circulating erythroblasts. Jaundice often occurred in the absence of or before the development of anemia, which casts some doubt on the usual explanation that jaundice and erythroblastemia are secondary to hemolytic anemia. Hemorrhagic manifestations were frequent, especially in infants with low prothrombin levels. Parenteral administration of vitamin K often had little effect on prothrombin levels. This fact, together with the poor correlation between the jaundice and anemia and the pathologic conditions in fatal cases, is evidence of poor hepatic function. The cause of hepatic damage is still unknown; perhaps it is arrested development of the liver in an immature phase or a direct effect of the antigen-antibody reaction. Patients with more impairment of hepatic function have deeper jaundice; those with better functioning livers may have little or no jaundice in spite of pronounced destruction of blood.

Complications were nonspecific diarrhea in 19 patients, obstructive jaundice in 3, septicemia in 2 and spasticity in one. The mortality was 35 per cent, with hemorrhage, atelectasis or bronchopneumonia frequent observations, as well as extramedullary hemopoiesis and hepatic necrosis. In only 2 cases did anemia appear to be a contributing cause of death. Edema and severe or increasing erythroblastemia indicated a poor prognosis.

Transfusion was the chief method of treatment. Comparison of results following use of Rh-positive and Rh-negative blood showed a similar immediate effect in raising the blood level and in improving the clinical condition, but Rh-negative blood resulted in fewer transfusion reactions and in a better sustained rise in hemoglobin. The necessity for immediate transfusion in nonanemic infants was questioned. In babies with good general condition it was recommended that frequent blood counts be done, and Rh-negative blood transfusions be given only if the hemoglobin fell below 11 Gm. In the absence of anemia, occasional infusions of plasma may be used for supportive effect and to prevent hemorrhagic tendencies. In critically ill infants, small transfusions of freshly drawn Rh-negative blood are advised. Vitamin K should be given frequently until the prothrombin level is normal. Additional therapeutic measures used in these cases—a high protein, high carbohydrate, and low fat formula (powdered half-skimmed milk with added carbohydrate), and administration of choline and liver extract—have a rational basis and warrant further trial. Administration of vitamin K to Rh-negative donors before drawing their blood was suggested as a means of raising the prothrombin level of affected infants and preventing hemorrhage.

AUTHOR'S ABSTRACT.

ANEMIA OF THE NEWBORN: A CASE REPORT. JOHN T. LESLIE, J. Pediat. **27**:265 (Sept.) 1945.

A case of anemia in a full term newborn boy is reported. There was 1 other child in the family, but the family history was entirely noncontributory. The infant was pale from the time of birth, but otherwise presented no abnormalities. On the fifth and sixth days the mother noticed momentary twitchings of the left extremities. On the seventh day the infant had generalized clonic convulsions, after which he appeared extremely pale, but otherwise an examination showed him to be normal. At this time the red blood cell count was 1,540,000 per cubic millimeter, but other laboratory observations, including, urinalysis and determination of blood calcium, leukocyte count, red cell morphology and clotting and bleeding times were normal. Three blood transfusions were given during the next four days, bringing the red

cell count up to a satisfactory level. After this the baby did well, but he had to be maintained with blood transfusions for two and one-half months until he was apparently able to generate a normal amount of his own blood. He received six transfusions with a total of 500 cc. of citrated blood during this period. Preparations of iron and liver extract were given but probably had no influence on the condition. The baby was followed for one year, during which time frequent blood, reticulocyte and platelet counts were done. Red blood cell fragility was normal. The mother's blood was Rh negative, the father's Rh positive and the baby's Rh positive; however, there were no observations which suggested the Rh factor as being of etiologic significance. The case might be classified as congenital hypoplastic anemia of the newborn.

Many textbooks and reports in the current literature continue to be confusing in classifying anemia of the newborn. It is felt that if the many unusual cases which occur are reported and if a careful analysis of them is made, these procedures will in the course of time aid materially in clarifying and solving the problem of that all-inclusive condition termed anemia of the newborn.

AUTHOR'S ABSTRACT.

REPORT ON AN OUTBREAK OF EPIDEMIC DIARRHEA OF THE NEWBORN. K. I. CAMPBELL, M. J. Australia **1**:79 (Jan. 27) 1945.

Experiences with three outbreaks of epidemic diarrhea of the newborn are recorded. The cases were noted between May 11 and August 2 (Australian winter months). Most infants were premature. Most were breast fed at onset. The artificially fed were on a diet consisting of a boiled milk and lactose dilution. The onset was sudden, with a slight rise in temperature and then the characteristic profuse watery diarrhea. No fecal material was present and blood was seen in the cases of only 2 infants who survived for seven days. Dehydration was alarmingly rapid. In some patients a nasal discharge was present. They were treated by parenteral administration of 5 per cent dextrose in isotonic solution of sodium chloride so as to supply 2 to 3 ounces (57 to 85 Gm.) of fluid per pound (454 Gm.) of body weight in twenty-four hours. Subcutaneous was found to be just as effective as intravenous administration. After a brief period of starvation dilutions of sweetened condensed milk were fed. Sulfathiazole was tried in one series, and the impression was that there was no benefit. In another series sulfaguanidine was used, and here the impression was that great benefit resulted. The larger dose gave the best results (0.5 Gm. followed by 0.25 Gm. every three hours).

Bacteriologic studies were made but showed the same flora as in 50 healthy infants. During the time of these epidemics cases of "gastric flu" were common in the city.

Interesting studies have shown that severe diarrhea can be produced by instilling either filtered or unfiltered stool materials from diarrheal infants into the nasal passages or stomach of calves.

The method of control used was to create three nurseries under separate staffs.

1. The isolation ward into which all afflicted infants were immediately placed.

2. The original nursery where all infants present at the start of the outbreak were kept until the normal time for their discharge.

3. A "clean" nursery for all infants born after the start of the outbreak.

Prompt action in combating dehydration and the liberal use of sulfaguanidine are considered most important in treatment.

TENNEY, Madison, Wis.

SEVERE PRIMARY ANEMIA IN THE NEWBORN. A. V. RAMÓN GUERRE, C. GIANELLI and R. DEAGUSTINI, Arch. de pediat. d. Uruguay **12**:217, 1941.

After a careful discussion of anemias and erythroblastosis in the newborn, the authors present a case of essential anemia in a newborn infant with healthy parents. The illness lasted a year and disappeared, not being influenced by any medication. The child's growth was excellent.

LOZOYA, México D. F., Mexico.

PRIMARY ILEITIS IN CHILDREN. ALBERTO LAGOS GARCÍA and C. J. GARCÍA DÍAZ, Arch. argent. de pediat. **14**:281, 1943.

This is a report of 5 cases of acute primary regional ileitis in 9 to 12 year old children.

All patients were operated on under the diagnosis of acute appendicitis, and the mistake was discovered at the operating table. This is a justifiable mistake because the morbid entity simulates an acute appendicitis. Crohn in 1932 showed that many obscure abdominal pictures were not due to appendicitis but to the beginning of a regional ileitis. Some other considerations related to the etiology and pathology are given by the authors.

LOZOYA, México D. F., Mexico.

PSEUDOSYPHILIS OF THE SKELETON IN THE NEWBORN. S. VAN CREVELD, Maandschr. v. kindergeneesk. **10**:129 (Jan.) 1941.

In the diagnosis of congenital syphilis great significance is ascribed to osseous lesions as revealed by roentgenograms. At the same time the question is raised as to how far these changes obtained by roentgen examination can be regarded as specific. It is pointed out, and illustrated by data from the literature, that several greatly varying conditions exist in which changes in the bones are visible in the roentgenograms, which can scarcely or not at all be distinguished from those which for many years have been considered as specific for congenital syphilis.

A description is given of a newborn baby, showing clinically the picture of the pseudoparalysis of Parrot, whereas roentgenologically a slight osteochondritis and a periostitis callosa could be ascertained. However, a syphilitic causation could be excluded, and the periostitis callosa was regarded as being caused by trauma.

AUTHOR'S ABSTRACT.

Acute Infectious Diseases

RHEUMATIC FEVER. WILLIAM WESTON JR., South. M. J. **38**:189 (March) 1945.

The author gives a brief general review of the subject in which he emphasizes the occurrence of rheumatic fever in the Southern states. He points out the value of prophylaxis with sulfadiazine and suggests the establishment of community clinics for treatment of rheumatic fever under competent medical and pediatric supervision.

LOGAN, Rochester, Minn.

FULMINATING MENINGOCOCCEMIA (THE WATERHOUSE-FRIDERICHSEN SYNDROME). H. R. PRATT-THOMAS, W. H. KELLEY and P. C. Gazes, South. M. J. **38**:229 (April) 1945.

A report of 4 cases (3 of adults and 1 of a child) and a brief review of the literature are given by the authors. One of the adults recovered following the prompt institution of treatment with sulfadiazine administered intravenously, sodium adrenal cortex extract and antimeningococcus serum. Reports of autopsies are presented. The cause of death is speculative but seems most likely to be the result of the septicemic process as a whole rather than of adrenal damage per se. Other organisms than the meningococcus may be encountered as etiologic agents in this syndrome.

LOGAN, Rochester, Minn.

ANCYLOSTOMA IN NURSING CHILDREN. MARIO V. FURQUIM, Arq. de pediat. **15**:29, 1943.

The finding of ancylostoma in nursing children is not rare, the incidence amounting to 9 to 26 per cent according to Brazilian statistics. It was found even in children 1 or 2 months old. The examination of the feces should be routine, especially if anemia is present.

LOZOYA, México D. F., Mexico.

CALCIUM AS A MEANS OF REACTIVATION OF MALARIA. E. J. ZAGURY, J. de pediat. **10**:35 (Feb.) 1944.

The author points out the utility of calcium injected intravenously, as an aid in investigation for plasmodiums in apparently healed patients.

LOZOYA, México, F. D., México.

Diseases of Blood, Heart and Blood Vessels and Spleen

HAND-SCHÜLLER-CHRISTIAN DISEASE. E. G. HUMMEL, J. Pediat. **26**:501 (May) 1945.

Until 1935 there had been reported only 60 cases of Hand-Schüller-Christian disease. Since that date a number of additional ones have been described. The first clinical description was made by Dr. Alfred Hand in 1895 before the Philadelphia Pathological Society. His observations were elaborated on by Dr. Christian in 1919 and Dr. Roland in 1928 (cited by Tannhauser, S. J.: Lipidoses: Disease of the Cellular Lipoid Metabolism, edited by Dr. Henry A. Christian [reprinted from Oxford Loose-Leaf Medicine], New York, Oxford University Press, 1940, p. 132). Because of the interesting characteristics of this case, I am presenting another one of these apparently infrequent lipid dystrophies.

F. L. Jr., a white boy, was a normal baby at birth, weighing 6 pounds and 13 ounces (3,100 Gm.). At 8 months of age he was somewhat thin and small featured and pale but never sick. At 2½ years of age, he was admitted to the hospital for study. At that time he was drinking 1 gallon of water daily and passing great quantities of urine. The report indicated that he had a disorder of the pituitary function at that time. At 6 years of age he came under my care at the Cooper Hospital. The roentgenogram of the skull showed a normal sella turcica. The diagnosis at that time was hypopituitarism and diabetes insipidus. When he was 8 years of age, blood transfusions were begun because of severe anemia; he has received twelve to date. The red cell count has ranged from 1,700,000 to 4,100,000.

Physical Examination.—He was examined again on April 13, 1944. His age was 9 years, his weight 27 pounds (12.2 Kg.) and his height 33¾ inches (84 cm.). The following observations were of special interest—eyes: slight exophthalmos; mouth: occasional bleeding gums—gingivitis; heart: no enlargement, the sounds forceful and of good quality with no murmurs and the P wave in lead II accentuated; blood pressure: 84 systolic and 68 diastolic; abdomen: pot bellied; skin: extremely pale, yellow, coarse and dry; extremities: legs long in comparison to the body and arms infantile.

Laboratory Studies.—The following results were of special interest—urine: albumin, a moderate trace, 5 to 6 red blood cells per high power field, 3 hyaline and 2 granular casts; blood count: 2,780,000 red blood cells per cubic millimeter; hemoglobin level 8.2 Gm. (49 per cent); 5,032 neutrophils (37 per cent); 13,600 white blood cells with 6,392 lymphocytes (47 per cent); 544 monocytes (4 per cent), 1,496 eosinophils (11 per cent), 136 basophils (1 per cent) and 1 Howell-Jolly body; 1 per cent of reticulocytes, and 94,520 platelets; blood urea nitrogen: 55 mg. per hundred cubic centimeters; blood urea acid: 8.2 mg. per hundred cubic centimeters; blood cholesterol: 516 mg. per hundred cubic centimeters.

Biopsy of the Sternum.—A microscopic examination of the section made June 1, 1944, revealed a somewhat fibrous marrow. Hemopoiesis was active, and cells of the eosinophilic series were particularly numerous. Scattered reticulum cells had a vacuolated cytoplasm suggesting lipid content.

Roentgenologic Studies.—These were made Nov. 26, 1940. The epiphyses for the heads of the femurs and humeri showed areas of lessened density, probably due to endocrine dysfunction. No evidence of rickets or scurvy was noted.

Further roentgenologic studies were made on April 15, 1944. There was decalcification of the osseous structure about the epiphyses of the shoulder girdle

and hip joint. There was likewise decalcification about the bones of the knee joints, as well as about the bones of the hands, but this was present without any complicating destruction or loss of outline of the bone contour.

At the time of the report the boy was 9 years of age, seemingly in good health, back in school after one year's absence and in the fourth grade. The presence of coronary disease, high blood urea nitrogen content and persistently recurring anemia, relieved only by blood transfusions, adds seriousness to this case.

Summary and Conclusion.—A case has been reported, believed to be the Hand-Schüller-Christian disease, based on the following diagnosis: (1) diabetes insipidus; (2) dwarfism; (3) high level of blood cholesterol; (4) exophthalmos; (5) high blood urea nitrogen content; (6) electrocardiographic evidence of coronary disease and intermittent gingivitis (frequent observations in this disease), and (7) roentgenologic studies of the bones and sternal biopsy compatible with this diagnosis.

AUTHOR'S ABSTRACT.

ACUTE HEMOLYTIC ANEMIA OF TYPE LEDERER-BRILL. KONRAD MEIER, Ann. pædiat. **162**:140 (Feb.-March) 1944.

The author gives a detailed description of acute hemolytic anemia (Lederer-Brill) from 2 cases observed by the author and from the literature. This disease is a rapidly progressing anemia of hyperchromatic character, with signs of good regeneration of the marrow of the bones. In 1 case spherical cells were observed which disappeared after complete recovery. Pathogenetically, relations to hemolytic icterus are assumed, and similar factors can provoke the crisis when there is a temporary endogenic disposition. The cure is transfusion of blood.

AUTHOR'S ABSTRACT.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

CONGENITAL DIAPHRAGMATIC HERNIA IN A CHILD WITH PULMONARY TUBERCULOSIS. AGUILAR, TORRES DE ANDA, LOZOYA and QUINTANAR, Bol. méd. d. Hosp. inf., México **3**:167 (July) 1945.

The patient reported on in this article was a girl 5 years of age, who was first seen in the outpatient department, where the tentative diagnosis of pulmonary tuberculosis and pleurisy of the left lung, with effusion, was made.

The author was somewhat confused by the clinical observations and the various roentgenograms; hence he ordered a tomography of the lower left lung, which revealed the presence of a portion of the small intestine and colon within the thoracic cavity. The child was operated on by the thoracic route. The chance for recovery was rather hazardous at first, but with the known therapeutics, such as oxygen, nikethamide, sulfadiazine and penicillin, the postoperative course was controlled.

The patient is still under treatment for pulmonary tuberculosis.

MADERO, México, D. F., Mexico.

ON JUDGING OF INDICATIONS OF OPERATING ON PYLORUS ACCORDING TO ROENTGEN EXAMINATION FINDINGS. ALICE LENZLINGER, Ann. pædiat. **161**:13 (July) 1943.

The author concludes that there is a fundamental necessity for roentgen examination of every stenosis of the pylorus. In 36 cases of stenosis of the pylorus roentgen examination was made. In 22 cases an operation was found to be necessary, and in 14 an operation was rejected. The good success of the treatment in both groups justified the decisions reached. Roentgen examination permits immediate and definite decision as to the treatment to be given. Thus, harmful loss of time, which worsens the state of nutrition and may endanger the success

of operation, is avoided. On 3 occasions accompanying cardiospasms were discovered; once cardiospasm and once stenosis as the cause of vomiting was revealed.

AUTHOR'S ABSTRACT.

ENDEMIC ENTEROCOCCIC INFECTION IN INFANTS AND LARGER CHILDREN. E. MAYERHOFER and N. KOVAČEVIĆ, Ann. pædiat. **161**:96 (Aug.) 1943.

The authors report an epidemic of an endemic "infectious intestinal catarrh." In 10 cases (children and infants) enterococci were established (in blood, feces and sputum). Most of the infections were severe; 3 of them—1, enterococcic sepsis—proved fatal. The symptomatology is variable and not pathognomonic. Sulfacetimide proved a good remedy. In outpractice, when neither bacteriologic nor serologic examination is possible, the authors recommend the use of sulfacetimide in tablet form in severe cases of intestinal catarrh not amenable to the usual treatment.

AUTHORS' ABSTRACT.

PSEUDO PYLORUS STENOSIS IN INFANTS WITH DIABETES SALINUS AS A RESULT OF ADRENAL HYPERTROPHY AND ENCEPHALITIS VIRCHOW. GERTRUD SCHACHENMANN AND HANS ZOLLINGER, Ann. pædiat. **163**:129 (Aug.-Sept.) 1944.

A 2 week old boy became ill with the symptoms of pyloric stenosis, was severely dystrophic and had a series of severe eruptions of seborrheic dermatitis. The usual treatment for pyloric stenosis was ineffective. A chronic hyposalemia, with good salt excretion in the urine was the most prominent symptom. A few acute catastrophies occurred, which were considered manifestations of coma hypochloremicum. Definite improvement of the condition and of the serologic manifestations was obtained by administration of isotonic solution of sodium chloride combined with desoxycorticosterone acetate. There was terminal infection of the urinary canal and death occurred in coma hypochloremicum after stopping the administration of isotonic solution of sodium chloride.

The postmortem examination showed hypertrophy of the cortex of the adrenal glands with poverty of lipid, and premature physiologic cortical changes. A chronic encephalitis, with abundant fat horn cells, was found.

Pathologists expressed the opinion that the encephalitis was prenatal in origin and therefore, in a manner, analogous to encephalus and other brain malformations, caused an early change in the adrenal cortex, which then produced the inferiority of the cortex cells. The hypertrophy of the cortex cells is to be considered the body's attempt to get rid of the cerebrally conditioned inferiority of the adrenal cortex cells. That this attempt was a failure is shown clinically and anatomically (by diabetes salinus and poverty of lipids in the adrenal cortex cells respectively).

AUTHORS' ABSTRACT.

Nervous Diseases

SALMONELLA CHOLERAE SUIS MENINGITIS. ERWIN R. NETER, Arch. Int. Med. **73**:425 (May) 1944.

Neter reports the case of a white girl aged 3 years and 11 months who was blind and hydrocephalic. Bacteremia and meningitis developed. Cultures of the blood and the cerebrospinal fluid revealed the presence of many gram-negative bacilli, which were identified as Salmonella cholerae suis (Salmonella suipestifer). Examination of the feces failed to reveal paratyphoid bacilli. The serum of the patient failed to show the presence of specific agglutinins. Sulfadiazine therapy was instituted, but in spite of this treatment the child died the following day. Cultures of the stools of the child's father, mother and brother failed to show evidence of paratyphoid bacilli, and agglutinins against the patient's strain could not be demonstrated in their serum.

The author reviews 78 cases of Salmonella meningitis described during the past twenty years. Twelve different species and types of Salmonella have been encoun-

tered in the past as the causative agent. These represent only a fraction of the species known to be pathogenic to man. Not a single case of meningitis due to the paratyphoid A bacillus is included in the group. Members of group B of the genus Salmonella account for 26, or one third, of all cases. Only 5 cases of meningitis were caused by Salmonella cholerae suis, the sole representative of group C; more than one-half of all instances of Salmonella meningitis were due to members of group D. Group E is represented by Salmonella sp. (London type) in a single case.

The author concludes that the prognosis of Salmonella meningitis is poor, but a few cases with recovery have been reported. No conclusions with respect to the efficacy of sulfonamide compounds can as yet be drawn, and they are not equally effective toward all species and types of the genus Salmonella.

GUTTMAN, Philadelphia [ARCH. NEUROL. & PSYCHIAT.]

MENINGITIS AND SULFATHIAZOLE. H. L. HOYNE and A. GRASSMAN, Arch. Pediat. **62**:241 (June) 1945.

A series of 137 cases of meningococcic meningitis representing all age groups, in which the patients were treated with sulfathiazole is reported. Twenty-seven deaths, 14 within thirty-six hours of admission to the hospital, occurred. The average patient had been ill four days when treatment was instituted.

The authors conclude that sulfathiazole is a valuable drug in the treatment of this disease, in spite of relatively low and variable concentrations in the blood and cerebrospinal fluid. Fewer toxic reactions were encountered than with sulfadiazine.

GRULEE, JR., Minneapolis.

ELECTROENCEPHALOGRAPHIC FINDINGS DURING AND AFTER ACUTE ENCEPHALITIS AND MENINGO-ENCEPHALITIS. IRA ROSS, J. Nerv. & Ment. Dis. **102**:172 (Aug.) 1945.

This is a report on the cerebral electroactivity in 4 cases of encephalitis and meningoencephalitis during the acute stage. The ages of the patients and the underlying causes of the disease were as follows:

A boy aged 18. The cause, measles.

A girl aged 2½ years. No definite etiologic factor. An infection of the upper respiratory tract preceded the syndrome.

A boy, 8 years old. A complication following tonsillitis.

A girl aged 10 years. Typhoid vaccine given five days preceding the onset of the neurologic symptoms.

The cerebral electroactivity was grossly disturbed. The abnormality was generalized and consisted of slow, bilaterally synchronous waves of enlarged amplitudes. The electroencephalographic disturbances were not proportional to the severity of the clinical picture. The findings generally are described as nonspecific. They simulate the dysrhythmia of any convulsive disorder or of a brain tumor.

JAHR, Omaha.

ENCEPHALO-TRIGEMINAL ANGIOMATOSIS. JOHN R. GREEN, J. Neuropath. & Exper. Neurol. **4**:27 (Jan.) 1945.

Green reports a case of a 3 year old boy who had a "port-wine birthmark" over the right frontal and parietal regions, including the area supplied by the first two divisions of the trigeminal nerve on that side. He had frequent and severe left-sided jacksonian seizures, which began after the age of 6 months. In addition, there were left hemiparesis, hemiatrophy of the left side of the body and mental retardation. An area of nonactivity was localized by electroencephalographic study in the right postparietal region. Roentgenograms of the skull revealed marked asymmetry, the left side being larger than the right. Sinuous, double-contoured calcifications were

present in the right anterior parietal region. Pneumoencephalograms showed marked atrophy of the right cerebral hemisphere and moderate dilatation of the right lateral ventricle. Stereoscopic arteriograms revealed increased vascularity and an abnormal tangle of small vessels in the distribution of the middle internal frontal, posterior internal frontal, paracentral and superior parietal branches of the right anterior cerebral artery and of the posterior parietal and central branches of the right middle cerebral artery. There were decreased circulation time through the same vessels, incorporation of the areas of calcification into the terminal distribution of the right superior and posterior parietal arteries on the right side and upward deviation of the terminal portion of the right anterior cerebral artery. Craniotomy was performed, and a hemangioma in the right parietal region was removed. The postoperative course was uneventful; the youngster improved, and the seizures were controlled with phenobarbital.

Green concludes that angiomatosis of the scalp, meninges and brain should be suspected when a child who has a "port-wine mark" in the area of the trigeminal nerve presents convulsions, hemiparesis or mental retardation. The diagnosis is confirmed by the finding of sinuous, double-contoured calcifications in the roentgenograms of the skull. Localization of the pathologic process may be aided by electroencephalographic and pneumoencephalographic studies and, according to Green, should be confirmed by stereoscopic angiograms, especially in cases in which there is no gross calcification.

The characteristic calcifications which occur in the upper layers of the cortex probably represent calcareous degeneration of primary angiomas.

Green, though not unmindful of the contributions of Sturge, Kalisher, Weber, Krabbe and others, suggests that the classification of such conditions preferably be in accordance with descriptive anatomic and pathologic terms because of the variability of the clinical and pathologic pictures. A designation like encephalotrigeminal angiomatosis seems appropriate, rather than a contested combination of proper names.

GUTTMAN, Philadelphia [ARCH. NEUROL. & PSYCHIAT.].

CONGENITAL DERMAL SINUS AS A SOURCE OF MENINGEAL INFECTION: REPORT OF TWO CASES, ONE ASSOCIATED WITH RECURRENT MENINGITIS. J. I. WARING and H. R. PRATT-THOMAS, J. Pediat. **27**:79 (July) 1945.

In 1934 Walker and Bucy reported 7 cases of congenital dermal sinus which was situated in the midline of the back. From small dimples in the skin epithelial tubes extended through unfused spinal laminas to the meninges of the spinal cord and furnished pathways by which infection spread to these structures.

Since the lesion is uncommon and may be the route by which infection reaches the meninges, we have described 2 examples of this malformation in detail.

The first was that of a white girl 10 years of age who had been born with a cutaneous defect in the lumbar region thought to be associated with spina bifida. She suffered 3 attacks of meningitis in three years. At operation a dermal sinus was revealed which extended from the skin into the spinal canal passing through a defect in the fifth lumbar vertebra. Subsequently, an epidural lesion developed that necessitated drainage.

The second case was that of a white girl 16 months of age. She had always been healthy. An area of increased pigmentation whose center contained a dimple was present over the third lumbar vertebra. At operation a sinus was traced from the skin through a defect in the third lumbar vertebra to the dura. This was excised, and recovery was uneventful.

Histologically the sinuses consisted of epithelial tubes, the first being lined in its major part by ciliated pseudostratified columnar epithelium. Walker and Bucy have expressed the opinion that in embryologic development the cleavage between cutaneous and neuroepithelial ectoderm is incomplete at the point where the sinus occurs and the neural tube carries down an invagination of the skin. It is likely that any type of fetal epithelium may in certain circumstances develop columnar epithelium possessing cilia, which explains the presence of this type of cellular

structure in the first case. In this case also the complications that may supervene are illustrated and the importance of recognizing and treating this condition before infection develops is given emphasis.

AUTHORS' ABSTRACT.

Diseases of the Genitourinary Tract

PROSTATE AND SEMINAL VESICLE RESPONSE TO TESTOSTERONE PROPIONATE IN INTACT AND CASTRATE RATS. FRANCES H. STEADMAN and BORIS KRICHESKY, Endocrinology **37**: 89 (Aug.) 1945.

Both castrated and intact male rats have been treated with testosterone propionate for periods varying from one to seven weeks. Organ–body weight ratios were maintained at or above control levels in both the castrated and the intact animals for both the prostate gland and the seminal vesicle. Testis weight decreased greatly throughout the course of the experiments.

JACOBSEN, Buffalo.

RENAL FAILURE SIMULATING ADRENOCORTICAL INSUFFICIENCY. G. W. THORN, G. F. KOEPF and M. CLINTON JR., New England J. Med. **231**:76 (July 20) 1944.

A syndrome characterized by excessive loss of sodium, chloride and water, resulting in collapse and associated with renal disease rather than adrenal disease, is described. Adrenal cortex extract is of no value in correcting the mineral depletion of these patients, since the renal tubular cell on which the adrenal hormone normally exerts its effect is unable to respond to additional hormone.

At present there does not appear to be a specific pathologic change responsible for excessive sodium and chloride loss other than widespread renal damage, associated with extensive scarring and a few remaining hypertrophied glomeruli and dilated tubules. Less severe loss of sodium and chloride is not infrequently observed in patients with chronic nephritis, and striking benefit may follow the judicious use of small quantities of supplementary sodium chloride and sodium bicarbonate under these circumstances.

For convenience and for its therapeutic implication, a patient with chronic renal disease having evident signs and symptoms of sodium and chloride depletion may be said to be suffering from "salt-losing nephritis."

AUTHOR'S SUMMARY.

CRYPTORCHIDISM. GEORGE R. LIVERMORE, South. M. J. **38**:477 (July) 1945.

A brief discussion of the symptoms, diagnosis, complications, prognosis and treatment of this condition is given. The author wisely emphasizes the dangers of the hormonal treatment. He recommends the Torek operation or a similar type of operative procedure and suggests that the operation be done sometimes after the age of 4 or 5 years. Two case reports are added and in addition 3 others in the "Discussion (abstract)."

LOGAN, Rochester, Minn.

POLYCYSTIC KIDNEYS IN CHILDREN. M. FÈVRE and T. VAN HOA, Presse méd. **53**:106 (March 3) 1945.

The authors point out that a unilateral tumor in the abdomen is probably a polycystic kidney and that the most logical treatment is nephrectomy—after ascertaining the function of the other kidney.

DAFFINEE, Melrose, Mass.

WILMS' TUMOR. SALAS, Bol. méd. d. Hosp. inf., México **3**:121 (July) 1945.

A detailed macroscopic and microscopic description is given. The author also furnishes information on the development, frequency and prognosis and on other

conditions peculiar to this tumor. He also states Dr. Farber's rules, that apply to all tumors in infancy: (1) abstinence from unnecessary manipulations and palpations before the operation; (2) complete surgical extirpation after a brief period of efficient study (forty-eight hours at the most); (3) knowledge of the surgical technic and the therapeutics peculiar to infancy; (4) radium therapy, when indicated, after the extirpation of the tumor. A 60 per cent success may be expected by following these rules.

MADERO, México, D. F., Mexico.

RENAL NANISM AND ARTERIAL HYPERTENSION. Y. ROBERT, Ann. pædiat. **163**:37 (July) 1944.

The author reports the case of an 11 year old girl with high arterial pressure, right-sided hydronephrosis and nephrosclerosis, the commencement of which goes back to early childhood, without the appearance of any acute nephritic stage at the beginning. There was backwardness in weight and stature. The cause of the hypertension is discussed in relation to the hydronephrosis and nephrosclerosis. The syndrome is best explained by the diagnosis "chronic interstitial nephritis." There are analogies with Cushing's disease which point to the possibility of a diencephalopituitary origin of the interstitial chronic nephritis.

AUTHOR'S ABSTRACT.

INCONTINENTIA URINAE CAUSED BY AN ECTOPIC IMPLANTATION. A. W. GRIEP, Maandschr. v. kindergeneesk. **10**:277 (April) 1941.

The author gives a description of a case of incontinence of the urine in a girl 13 years old, caused by an ectopic implantation of the ureter. Heminephrectomy of the right kidney gave complete recovery.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Ductless Glands; Endocrinology

STUDIES ON THE HORMONAL CONTROL OF ESTROUS PHENOMENA IN THE ANESTROUS EWE. H. H. COLE, G. H. HART and R. F. MILLER, Endocrinology **36**:370 (June) 1945.

Injections of pregnant mare's serum, estrogens and testosterone propionate were used. Although estrus was induced by several methods in a high percentage of animals, a complete physiologic response was not produced regularly. The conclusion is reached that either a proper balance of hormones was not attained or unknown factors are involved.

JACOBSEN, Buffalo.

THE DISTRIBUTION OF CELL TYPES IN THE ANTERIOR HYPOPHYSIS DURING LATE PREGNANCY AND LACTATION. NEWTON B. EVERETT and BURTON L. BAKER, Endocrinology **37**:83 (Aug.) 1945.

Differential cell counts of hypophyses from pregnant and lactating rats show that at three days post partum the acidophils have increased by almost 100 per cent, above the number present in pregnant animals. This increase coincident with a reduction in the number of basophils during the period of great increase in lactogen indicates that the acidophils and not the basophils are probably responsible for the production of lactogen.

JACOBSEN, Buffalo.

THE CHOLESTEROL AND ASCORBIC ACID CONTENT OF THE ADRENAL, LIVER, BRAIN, AND PLASMA FOLLOWING HEMORRHAGE. GEORGE SAYERS, MARION A. SAYERS, TSAN-YING LIANG and C. N. H. LONG, Endocrinology **37**:96 (Aug.) 1945.

Following a nonfatal hemorrhage both the cholesterol and the ascorbic acid content of the adrenal glands of the rat are decreased. Hypophysectomy prevents

these alterations. The plasma ascorbic acid rises slightly after nonfatal hemorrhage and is increased sixfold in shock. It is suggested that the alterations in adrenal cholesterol and ascorbic acid are associated with the secretion of the cortical hormones and that they participate in their formation.

JACOBSEN, Buffalo.

STUDIES ON THE ROLE OF THE LIVER IN THE METABOLISM OF PROGESTERONE. G. MASSON and M. M. HOFFMAN, Endocrinology **37**:111 (Aug.) 1945.

In an experiment with the normal estrogen-primed immature rabbit, 200 mg. of progesterone had to be administered by gavage to obtain a progestational response comparable to that elicited by 0.25 to 0.5 mg. administered subcutaneously. In an experiment with the partially hepatectomized rabbit, on the other hand, comparable progestational changes were obtained by the administration of 25 mg. of progesterone by gavage. This striking decrease in the intragastric dose required to cause progestational proliferation is interpreted as indicating that the liver plays an important role in the inactivation of progesterone in the rabbit.

JACOBSEN, Buffalo.

VICARIOUS METABOLIC RESPONSE: THE INFLUENCE OF BLOOD FROM THYROXINIZED ANIMALS ON THE OXYGEN CONSUMPTION OF SURVIVING TISSUE. FRANCIS N. CRAIG and WILLIAM T. SALTER, Endocrinology **37**:117 (Aug.) 1945.

The iodine in the blood of subjects with hyperthyroidism tends to be abnormally high. It now appears that the blood of animals with hyperthyroidism can induce an elevated metabolic rate in surviving tissues excised from normal animals. Pure thyroxin added to normal mammalian blood does not induce this metabolic response, and thyroglobulin does not appear in systemic blood in quantities sufficient to be detected by immunologic methods.

These observations provide evidence for the view that the circulating thyroid factor is neither thyroxin nor thyroglobulin in pure form.

JACOBSEN, Buffalo.

ADRENAL MEDULLA IN WATER DIURESIS AND WATER INTOXICATION. ROBERT GAUNT, MILDRED LILING and MARGARET CORDSEN, Endocrinology **37**:136 (Aug.) 1945.

The fact that adrenalectomy reduces noticeably the diuretic response to water and increases the susceptibility to water intoxication has generally been attributed exclusively to adrenal cortical deficiency. The experiments here reported were devised to test the role of the adrenal medulla.

It is concluded that the effects of adrenalectomy on water excretion are not due in significant part to loss of the adrenal medulla and that any important physiologic role of epinephrine in water diuresis is not established by these experiments.

JACOBSEN, Buffalo.

STUDIES ON WATER INTOXICATION IN ADRENALECTOMIZED RATS AND THE INFLUENCE OF DESOXYCORTICOSTERONE ACETATE (DCA) AND EPINEPHRINE IN WATER DIURESIS. HARRY W. HAYS and DONALD R. MATHIESON, Endocrinology **37**:147 (Aug.) 1945.

Desoxycorticosterone acetate has been shown to be effective not only in maintaining the life of bilaterally adrenalectomized animals but in acting as a protective agent when both normal and adrenalectomized animals are subjected to excessive amounts of water by mouth.

In these experiments with both desoxycorticosterone acetate and epinephrine hydrochloride, there was definite protection from convulsion and death from water intoxication.

JACOBSEN, Buffalo.

DIABETES-LIKE CONDITIONS IN CHILDHOOD. T. THYSELL, Ann. pædiat. **160**:225 (May-June) 1943.

It may be said that there is probably no case of cured diabetes described in the literature. In children there appear transitory conditions with hyperglycemia, ketonuria and glycosuria which may give the impression of diabetes. In most of these cases it may be assumed that there was an encephalitic or toxic influencing of the carbohydrate-regulating brain centers. The infection is probably just as incapable of producing genuine diabetes as is trauma of the skull (Thomsen). However, the infection may, just as such trauma, occasionally aggravate a developing diabetes or bring to light a latent diabetes mellitus. In the case of temporary diabetes-like conditions, insulin treatment may have a certain value.

AUTHOR'S ABSTRACT.

Diseases of the Muscles, Bones, Joints and Lymph Glands

ROUND CELL TUMOR OF BONE RESEMBLING EWING'S TUMOR. ROBERT J. REEVES, South. M. J. **38**:302 (May) 1945.

The cases of 2 girls, one 9 years of age and the other 6 years of age, are reported. In the first case the primary tumor was in the area of the left lower bicuspid. There were multiple metastases, all of which were apparently cured by roentgen therapy. The patient was treated over a ten year period. In the second case the primary lesion was in a rib, with metastases throughout the lungs. Roentgen therapy was given without expectation of benefit. Eleven years later the patient was living and well.

LOGAN, Rochester, Minn.

13 CASES OF CENTRAL BONE ABSCESSES (BRODIE ABSCESS) IN CHILDHOOD WITH SPECIAL REFERENCE TO INFANTS. EDWIN SIGRIST, Ann. pædiat. **162**:113 (Feb.-March) 1944.

The author reports 12 of his cases of central bone abscess (the Brodie abscess), 6 of which were those of infants. While local pain, swelling and, when near the joint, loss of function were clinical hints, the diagnosis is made roentgenologically (bone cavity with sclerotic wall). The peculiarities in infancy are the relative frequency of initial forms, localization in the metaphysis and involvement of the joints. Perhaps many cases of benign pneumococcic monarthritis in the literature belong to this classification. Treatment consists of rest and protracted administration of sulfonamide compounds. An operation, especially in the initial stage, in the vicinity of the joint and in infancy has its dangers.

AUTHOR'S ABSTRACT.

Diseases of the Eye

CONGENITAL GLAUCOMA AND CATARACT, BILATERAL, GONIOTOMY AND NEEDLING. T. D. ALLEN, Am. J. Ophth. **28**:388 (April) 1945.

Allen cites the case of a 5 month old child with bilateral glaucoma and an associated cataract in which he did goniotomies by inserting the goniotomy knife at the limbus of the cornea and passing it across the pupil and sweeping down into the angle in the inferior nasal quadrant. Four operations were performed on the left eye. No contact glass was used. A single similar procedure was used on the right eye.

The tension when the patient was under narcosis was 31 and 46 mm. in the two eyes; this was reduced to 20 and 16 mm. of mercury. A single needling of the lens was done in each eye.

This method is not advocated as universally applicable in all cases of deep chamber glaucoma or in all cases of hydrophthalmos; it is merely intended to record what has been accomplished in this 1 case.

W. ZENTMAYER. [ARCH. OPHTH.]

SOME OBSERVATIONS ON DIVERGENT STRABISMUS WITH ANOMALOUS RETINAL CORRESPONDENCE. H. W. GRANT, Am. J. Ophth. **28**:472 (May) 1945.

Twenty-two cases of divergent strabismus with constant anomalous correspondence were studied from the standpoint of diagnosis and treatment. The fusion was so poor in some instances as to make the after-image test unreliable.

On the basis of the therapeutic results the cases are divided into three main groups: 1. Cases with poor convergence which was incurable, the deviation tending to assume its original amount and characteristics after surgical correction. Convergence exercises helped to reduce the cosmetic defect, but the improvement was not maintained.

2. Cases with good convergence in which the deviation could be corrected surgically. Severe asthenopic symptoms and incongruous diplopia were present for years after surgical correction.

3. Cases of horror fusionis with total or partial anomalous correspondence which was completely relieved by extreme care in correcting the refractive error.

W. S. REESE. [ARCH. OPHTH.]

THE CAUSE AND TREATMENT OF POOR VISION IN ANIRIDIA. L. G. ALGER, Am. J. Ophth. **28**:730 (July) 1945.

Alger believes that the reduced vision associated with aniridia is due to aberration of light in the region of the equator of the lens. He discusses methods used to overcome this and reports a case in which he tattooed the cornea.

W. S. REESE. [ARCH. OPHTH.]

DEVIC'S DISEASE. S. J. SILBERMAN, J. Nerv. & Ment. Dis. **102**:107 (Aug.) 1945.

A case of neuromyelitis optica in an 18 year old woman is presented, together with a comprehensive review of the literature of this peculiar disease.

JAHR, Omaha.

MEGALOCORNEA AND OSSEOUS DYSTROPHY. JOSE BANABA and CARLOS GARBINO, Arch. pediat. d. Uruguay **15**:493 (Sept.) 1944.

As an example of congenital mesodermal dystrophy the authors describe a peculiar association of anomalies in a girl 30 months of age. Manifestations included bilateral megalocornea, coloboma, refractive error, macular degeneration, osteoporosis and delay in skeletal growth and maturation without evidence of rickets. A familial pattern of inheritance was suggested.

PLATOU, New Orleans.

NEURORETINITIS AND MACULAR STAR. E. CAMPOS, Arq. brasil. de oftal. **5**:131 (June) 1942.

A patient 11 years of age had lost the sight of the right eye twelve days before examination. The conjunctiva, cornea and iris were normal. Isocoria was present. Vision was reduced to light perception, without light projection. A perfect macular star and pronounced edema of the disk were present. Small hemorrhagic foci were seen in the region of the edema. The patient's parents were syphilitic; as he showed physical stigmas of hereditary syphilis, although no evidence was obtained from the laboratory tests, a diagnosis of neuroretinitis with macular star, possibly of syphilitic origin, was made. The literature dealing with such cases is reviewed. A bibliography is included.

M. E. ALVARO. [ARCH. OPHTH.]

PHLYCTENULAR CONJUNCTIVITIS IN SCHOOL CHILDREN. RENE CONTARDO, ARTURO PERALTO S. and JUAN ARENTSEN S., Pediat. Américas **2**:402 (July) 1944.

The authors studied 7,200 school children from 1938 to 1941 (four years). They found that 376 (5.22 per cent) had phlyctenular conjunctivitis.

Of the patients for whom a roentgenologic examination revealed no abnormalities 185 (66 per cent) had positive reactions to tuberculin tests. Of the ones for whom roentgenologic examinations revealed abnormalities, 191 (92.63 per cent) had positive reactions to tuberculin tests (von Pirquet and Mantoux).

The sedimentation rate was high for 60 per cent of the patients with pulmonary lesions and for 71.4 per cent of the patients whose roentgenologic examination revealed abnormalities.

It was exceptional for the tuberculin reaction to produce any increase of symptoms.

The authors postulate that phlyctenular conjunctivitis must be interpreted as a specific allergic reaction to tuberculin in the majority of cases, and in those in which there is no tuberculosis, as a purely allergic reaction.

DE LA TORRE, Rochester, Minn.

Skin Diseases; Allergy

A DISCUSSION OF ANGIOMATA AND PIGMENTED NEVI. LEE BIVINGS, South. M. J. **38**:241 (April) 1945.

The author recommends cosmetic coverage for the flat type of angioma. For the hypertrophic type he recommends no treatment but to allow it to regress spontaneously. For the cavernous type he recommends surgical removal. Pigmented moles may be removed by electric desiccation or by surgical intervention if they are in locations apt to become irritated.

LOGAN, Rochester, Minn.

HYDROLABILITY AND DEATHS IN CASES OF ECZEMA. E. FREUDENBERG, Ann. pædiat. **162**:162 (Feb.-March) 1944.

The author reports a case of serious chronic infantile eczema which with a continuous loss of liquid led to death. The attempted treatment to stop the anhydremia, consisting of intravenous administration of isotonic solution of sodium chloride and of solution of dextrose, human blood plasma, sodium bicarbonate, insulin and desoxycorticosterone acetate, was of no use. An analysis of these phenomena is attempted, and a grave defect of the capillaries is assumed as the primary cause of these troubles.

AUTHOR'S ABSTRACT.

Teeth and Dentistry

THE RELATION BETWEEN FOOD AND CONDITION OF THE TEETH. B. C. P. JANSEN, Maandschr. v. kindergeneesk. **10**:295 (April) 1941.

Recent researches on food and metabolism have shown in animal experiments that in deficiency of ascorbic acid or of vitamin D an excess of fluorine in the food and other factors gives rise to all kinds of deviations of the normal construction of the teeth and in this way also to deviations of the normal resistance of the teeth. Numerous observations in men can also only be explained by assuming that the alarming frequency of caries in the civilized peoples is caused by food which in this respect is not optimal. However, much research work still must be done in order to give exact indication of which way the Dutch food should be modified or completed so that it will be the most favorable with respect to the condition of the teeth.

VAN CREVELD, Amsterdam, Netherlands.

DETERMINATION OF VERY SMALL AMOUNTS OF MOLYBDENUM IN BIOLOGIC MATERIAL. P. L. HOOGLAND and G. A. LAMPE, Nederl. tijdschr. v. geneesk. **88**:578 (June 17-24) 1944.

With a method described by the authors (*Arch. néerl. de physiol.* **27**:145, 1943), a method which allows a determination in about 1 Gm. of material, the amount of molybdenum in teeth and in molar teeth was determined separately. The opinion

of Ter Meulen (1935), that carious teeth contain much less molybdenum than noncarious teeth and that molybdenum might be of influence for the appearance of caries, was investigated. It appeared that carious and healthy teeth had the same molybdenum content (about 0.05 microgram per gram). Therefore the significance of molybdenum for the appearance of caries is doubted.

VAN CREVELD, Amsterdam, Netherlands.

Miscellaneous

A CASE HISTORY OF TWINS BREAST FED ON A SELF-DEMAND REGIME. GENEVIEVE TRAINHAM, GRACE J. PILAFIAN and RUTH M. KRAFT, J. Pediat. **27**:97 (Aug.) 1945.

This is a case history of the first thirteen months of life of fraternal twins, brother and sister, whose care was based on a philosophy emphasizing recognition of and adherence to individual needs. The history includes 2 tables, one showing the length and weight of both infants at birth and at 3, 6, 9 and 13 months and the skeletal age (Todd standard) at 3, 6, 9 and 13 months and the other showing the children's developmental rating (Gesell standard) at 28 weeks and at 13 months. Throughout the account the feeding history of the infants receives the major emphasis. Two graphic charts show the feeding schedules set up by the infants themselves on the self-demand regimen, which was initiated at the end of the thirteenth day.

Peter, weighing 8 pounds, 5 ounces (3,770 Gm.) at birth, and Sherry, 5 pounds, 9½ ounces (2,540 Gm.) during their thirteen days in the hospital were nursed on a four hour schedule. When self demand was initiated at home and the infants were permitted to sleep or to nurse at will, each infant dropped the sixth feeding at once except occasionally, and, indeed, frequently demanded only four feedings in twenty-four hours. By the eighth week the day of five feedings had almost completely disappeared, and from the ninth week the day of three feedings was frequent. From the sixteenth week for Peter and the seventeenth for Sherry, the latter was the usual feeding demand. There was an increasing regularity of the feeding interval for each infant, with some schedule apparent even in the third week. This beginning schedule was so unlike that of the hospital days as to suggest that the hospital routine had no influence on its emergence.

Solid foods, begun at 2 months, were quickly accepted by both babies.

To prepare the babies for weaning, orange juice was given from a cup beginning at 3 months, and during the seventh month a small amount of milk from a cup was occasionally offered between feedings. At the end of the thirty-second week milk from a cup was substituted for breast milk at the noon feeding and readily accepted by each infant. Other breast feedings were rejected by the babies themselves: first, the morning feeding and, finally, the evening feeding. Peter refused the latter at 9 months of age and Sherry at 10½.

Charts are included showing the daily total sucking time of each baby for a period of thirty-five days and the frequency distribution of individual sucking periods according to length in minutes. Each infant was allowed to nurse at any time as long as it desired, and nursing periods ranged from three minutes to fifty-five. Peter's median sucking time during the thirty-five day period recorded was twenty-four and five-tenths and Sherry's twenty-one and six-tenths minutes. Sherry has never sucked her thumb, while Peter sucked his almost constantly at 4 months and in moments of stress still did so at 13 months.

For both babies gains in length, weight and skeletal age have been satisfactory, and developmental progress has been superior.

Two factors contributed largely to the mother's success in nursing twins in this manner: first, psychologic readiness and, second, excellent nutrition throughout the prenatal and lactating periods.

AUTHORS' ABSTRACT.

DISCUSSION ON THE SCHOOL MEDICAL SERVICE, PRESENT AND FUTURE. Proc. Roy. Soc. Med. **38**:373 (May) 1945.

Dr. John D. Kershaw, in his discussion, points out that the self-contained school medical service has three main objectives: (1) the detection and care at the earliest possible stage of defects, diseases and tendencies to defect and disease, (2) the prevention of defects and diseases by such means as the development of school and personal hygiene, health education and the anticipation of malnutrition by the provision of milk and meals in school and (3) the most important of all, constructive work. Then follows in detail a variety of means by which these ends may be accomplished. He hopes in the future that there will be a closer understanding between university departments and institutes of child health and social medicine and school medical service.

Dr. Isobel Wright stated that the present supervision of the 2 to 5 year age group comprises (1) periodic home visits by a health visitor who advises on general hygiene, regimen and diet; (2) voluntary attendance at infant welfare centers for medical examination and periodic weighing; (3) day nurseries, and (4) nursery classes which are available at some of the ordinary elementary schools.

WILLIAMSON, New Orleans.

PENICILLIN: A SUMMARY OF ITS INDICATIONS AND DOSAGE. LÁZARO BENAVIDES and RODOLFO QUINTERO, Bol. méd. d. hosp. inf., México **2**:329 (Nov.-Dec.) 1945.

The authors begin this article with a brief and practical description of the most important things that should be known about penicillin, such as the Oxford unit, the lability, the dosage according to the type and the severity of the infection, the preparation for treatment and the different types and salts available. Then they describe the different routes used for the introduction of the drug into the organism. The last part of the article is dedicated to the indications. Also, the authors summarize those cases in which the action of the medicament has been void of effect.

MADERO, México, D. F., Mexico.

News and Comment

GENERAL NEWS

Physicians Certified by the American Board of Pediatrics.—The following physicians were certified as specialists by the American Board of Pediatrics, after examinations held at Cleveland April 27 and 28, 1946:

Dr. Herman Anfanger, Camp Forest, Tenn.; Dr. Richard Winston Blumberg, Fort Oglethorpe, Ga.; Dr. Moses R. Buchman, Scarsdale, N. Y.; Dr. Martha Louise Clifford, Hartford, Conn.; Dr. David Richard Davis, Emporia, Kan.; Dr. Paul A. di Sant'Agnese, New York; Dr. Elinor Fosdick Downs, New York; Dr. Jerome Feldman, Hoopeston, Ill.; Dr. Kurt Glaser, Chicago; Dr. Edward Alun Harris, Fairfield, Ala.; Dr. Scott Thurber Harris, Detroit; Dr. William W. Herman, Cleveland Heights, Ohio; Dr. Gertrude E. Howe, Chicago; Dr. Hyde S. Leland, Detroit; Dr. Leo Litter, New Britain, Conn.; Dr. Nina Litton, Boston; Dr. Erhard Loewinsohn, Chicago; Dr. Frederick J. Margolis, Kalamazoo, Mich.; Dr. David William Martin, West Palm Beach, Fla.; Dr. George Winford McCormick, Staten Island, N. Y.; Dr. Ralph E. Moloshok, New York; Dr. Marion Shaffner Morse, Endicott, N. Y.; Dr. Alexander Sandor Nadas, Greenfield, Mass.; Dr. Henry Bernard Okner, Chicago; Dr. Edward L. Pratt, Boston; Dr. Alexander E. Rostler, Fall River, Mass.; Dr. Herschel Sachs, Cincinnati; Dr. Edwin Paul Scott, Louisville, Ky.; Dr. Amelia Burns Sheftall (Geeslin), Jacksonville, Fla.; Dr. Bernard Harold Shulman, Brooklyn; Dr. Harold I. Shuman, Boston; Dr. William Benjamin Smith, Indianapolis; Dr. Stuart Shelton Stevenson, Fairfield, Conn.; Dr. Stewart C. Wagoner, Schenectady, N. Y.; Dr. Dwain Newton Walcher, New Haven, Conn.; Dr. Edwin Robeson Watson, Mobile, Ala., and Dr. B. H. Williams, Joplin, Mo.

Forty-nine physicians were examined at Cleveland. Of these, thirty-seven passed and were certified.

The following physicians were certified as specialists by the American Board of Pediatrics after examinations held at San Francisco, July 6 and 7, 1946.

Dr. Talcott Bates, Monterey, Calif.; Dr. Joseph Harold Batzle Jr., Riverside, Calif.; Dr. Louise S. Childs, Honolulu, Hawaii; Dr. Homer Tullock Clay, Tacoma, Wash.; Dr. Peter Cohen, San Francisco; Dr. Percy F. Guy, Seattle, Wash.; Dr. Alexander Hatoff, Oakland, Calif.; Dr. George D. Husser, Richmond, Calif.; Dr. Owen Austin Kearns, Monrovia, Calif.; Dr. Pearl Lee, San Bernardino, Calif.; Dr. Edward Augustus Loeb, Fontana, Calif.; Dr. Stanley Louie, San Francisco; Dr. Edgar L. Mariette, Glendale, Calif.; Dr. William W. Ornduff, Berkeley, Calif.; Dr. Lawrence E. Reck, San Diego, Calif.; Dr. James T. Stanton, Bakersfield, Calif.; Dr. Margaret Stebbins (Smith), Pittsburgh; Dr. Robert Austin Tidwell, Seattle, and Dr. Edwin Thurston Williams, Denver.

At San Francisco twenty-six physicians were examined. Of these, nineteen passed and were certified.

Book Reviews

Virus as Organism. Evolutionary and Ecological Aspects of Some Human Virus Diseases (Monograph in Medicine and Public Health, No. 8). By Frank M. Burnet. Price, $2.00. Pp. 134. Cambridge: Harvard University Press, 1945.

This book was reviewed by two persons interested in virology. All but the last paragraph was mutually agreed on. One reviewer insisted on the addition of the last paragraph despite the fact that it might be considered superfluous and not apropos.

In all fields of work where vast numbers of facts are accumulated, one must stop occasionally and try to interpret and to integrate them with a possible working hypothesis in view. The facts, when brought together into a satisfactory relationship, may point the way toward further progress. It does not matter whether the hypothesis is correct, so long as it is responsible for additional knowledge, which eventually may even render the original hypothesis untenable.

Burnet indulges in speculations about origins and changes in viruses and virus diseases from a biologic angle. He admittedly has taken the privilege and license of a lecturer and has gone somewhat beyond what would be permitted in general scientific writing.

Burnet's essential theme is that viruses are micro-organisms which have evolved from larger micro-organisms, mostly bacteria, by continued mutation and parasitic degeneration. With a background of ecology and evolution to bolster his point of view, he surveys viruses according to the primary biologic attributes, i. e., reproduction, variation, survival and evolution. He presents evidence to show that their behavior, their chemical structure and their general pattern of living material conforms with biologic concepts, although perhaps in a broad sense. He inferentially ignores new mechanisms.

He concludes that viruses, with time, have evolved with increasing simplicity of structure into a self-producing residuum of genetic mechanism. This theory is not new, but the author's presentation and treatment of the subject are the most complete up to the present. Even to one who believes that viruses are inanimate substances without the attributes of living things, this treatise and Burnet's concepts would not appear to influence the practical problems of viruses and their control. Viruses must be produced in one way or another and have a means of indefinite survival. Their production must occur either as entities which parasitize the host or as chemicals which behave like enzymic catalysts, whereby some dynamic mechanism replicates similar substances by the arrangement of suitable atomic groups within the cells. In either case their structures are reproduced at the expense of the susceptible host cells, with obvious clinical or pathologic manifestations of their activity. Their pathologic, epidemiologic and immunologic behavior is analogous to that of the known bacteria or protozoa.

Burnet's hypothesis has the essential attributes of any good postulation in its simplification of the trends of thought and opening of new pathways for experiment.

As stated in the foregoing comment, Burnet's purpose was to review all the accumulated work which would favorably demonstrate that viruses are micro-organisms and act like them. He does this so well and so plausibly that those of us who do not see eye to eye with him as to the living character of viruses may even be tempted to succumb to his blandishing arguments. This is an excellent book for its purpose, and gives in detail all of the arguments of the biologist who believes that the viruses are living entities, but it does not convince the skeptical, to which group one of the reviewers belongs.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-General: Dr. L. Emmett Holt Jr., 477 First Ave., New York 16.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto 2.
Secretary: Dr. S. G. Ross, 1390 Sherbrooke St. W., Montreal.
Place: New York. Time: Sept. 16-19, 1947.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

Save the Children International Union

President: Mrs. Gordon Morier.
Secretary: Dr. Georges Thélin, 43 Quai Wilson, Geneva, Switzerland.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

Associação Paulista de Medicina, Secçaõ de Pediatrias

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Luiz Augusto Monteiro Toledo, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.
Time: Twelfth of every month, 8:30 p. m.

British Paediatric Association

President: Prof. G. B. Fleming, 13 Lynedoch Crescent, Glasgow.
Joint Secretary: Prof. Alan Moncrieff and Dr. Donald Paterson, Hospital for Sick Children, Great Ormond St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandische Vereeniging voor Kindergeneeskunde

President: Dr. J. H. G. Carstens, Servaas Bolwerk 14, Utrecht.
Secretary: Dr. R. P. van de Kasteele, Lyccumplein 10, den Haag.
Place: Children's Hospital or Pediatric Clinic. Time: Three times a year.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. L. F. Meyer, 29 Toelsohn St., Tel Aviv.
Secretary: Dr. A Brünn, 9 Maazestre, Tel Aviv.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Prof. Norman Capon, 49A Rodney St., Liverpool, England.
Secretary: Dr. J. N. O'Reilly, 46 Harley St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

SOCIEDAD CUBANA DE PEDIATRIA

President: Dr. Teodosio Valledor, Habana.
Secretary: Dr. Carlos Hernandez Miyares, Hospital Nuestra Señora de las Mercedes L y 21, Apartado, 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Nuestra Señora de las Mercedas y Hospital Municipal de Infancia, Habana. Time: Last Wednesday of every month.

SOCIEDAD ECUADORIANA DE PEDIATRIA

President: Dr. Francisco de Icaza Bustamente.
Secretary: Dr. M. I. Gómez Lince, P. O. Box 693, Guayaquil.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Luis Berlanga Berumen, Bucareli No. 85, Altos, Mexico.
Secretary: Dr. Jésus Alvarez de los Cobos, Ignacio Mariscal 124, Mexico.

SOCIEDAD DE PEDIATRIA DE CÓRDOBA

President: Dr. Juan Francisco Herrera, Córdoba, Argentina.
Secretary: Dr. Bernardo Serebrinsky, Dean Funes 2000, Esq. Ocaña (N.), Córdoba. Argentina.
Place: Comite pro Defenso del Niño, Dean Funes 2000, Córdoba, Argentina. Time: Once a month.

SOCIEDAD DE PEDIATRIA DEL LITORAL

President: Dr. Jose E. Celoria, Hospital Centenario, Rosario, Argentina.
Secretary: Dr. Gloria Lovell, Hospital Centenario, Rosario, Argentina.

SOCIEDAD DE PEDIATRÍA DE SANTIAGO DE CUBA

President: Dr. Antonio Béguez César, Sagarra 107, Santiago de Cuba.
Secretary: Dra. Susana Texdó Vaillant, Padre Pico 57, Santiago de Cuba.
Place: Colegio Médico. Time: Last Tuesday of every month.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. Pedro J. Alvarez.
Secretary: Dr. Ernesto R. Figueroa, 3a Avenida 10, Bella Vista, Caracas.
Place: Hospital Municipal de Niños Jose Manuel de los Rios, Caracas.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. Leveuf, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Maladies, 149 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

SWEDISH MEDICAL SOCIETY, SECTION FOR PEDIATRICS AND SCHOOL HYGIENE

President: Prof. Arvid Wallgren, 53 Strandvägen, Stockholm.
Secretary: Dr. Henning Magnusson, 58 Odengatan, Stockholm.
Place: Various clinics and hospitals in Stockholm and Uppsala. Time: Second Friday of each month (except summer).

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Jose Bonaba, Montevideo.
Secretary: Dr. Héctor Fossatti, Durazno 1882, Montevideo.
Place: Club Medico del Uruguay, Avenida Agraciado 1464 (Piso 13), Montevideo

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. Jay I. Durand, 515 Cobb Bldg., Seattle, Wash.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Hotel William Penn, Pittsburgh. Time: Nov. 13-16, 1946.

AMERICAN HOSPITAL ASSOCIATION, MASSACHUSETTS HOSPITAL ASSOCIATION

Chairman: Dr. Frank Wing, Boston.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly 79, Mass.
Place: Boston. Time: November 1946.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Harold K. Faber, 2361 Clay St., San Francisco.
Secretary-Treasurer: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. H. S. Little, 300 Dufferin Ave., London, Ontario.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, 67 College St., Toronto 2.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Mitchell I. Rubin, 219 Bryant St., Buffalo 9, N. Y.
Secretary: Dr. Robert F. Ward, Bellevue Hospital, New York 16.

SECTIONAL

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Robert Alway, University of Utah School of Medicine, Salt Lake City 2.
Secretary-Treasurer: Dr. L. Paul Rasmussen, 1020 Boston Bldg., Salt Lake City 1.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Secretary-Treasurer: Dr. Charles D. May, 300 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Three meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. Percy Guy, 502–2d Ave., Seattle, Wash.
Secretary: Dr. Aldis B. Johnson, 515 Cobb Bldg., Seattle, Wash.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. George Kimmel, Redwing, Minn.
Secretary-Treasurer: Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver 2.

SOUTHERN MEDICAL ASSOCIATION, SECTION OF PEDIATRICS

Chairman: Dr. Stewart H. Welch, 117 S. 20th St., Birmingham 5, Ala.
Secretary: Dr. W. Ambrose McGee, 1601 Monument Ave., Richmond 20, Va.
Place: Miami, Fla. Time: Nov. 4-7, 1946.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Jerome C. Chapman, 2160 Highland Ave., Birmingham.
Secretary-Treasurer: Dr. Ruth Berrey, 2021–6th Ave. N., Birmingham.

ARIZONA PEDIATRIC SOCIETY

President: Dr. W. P. Sherrill, 342 W. McDowell Rd., Phoenix.
Secretary: Dr. W. F. Schoffman, 926 E. McDowell Rd., Phoenix.
Place: Phoenix or Tucson. Time: At time of state meeting.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco 9.
Secretary: Dr. Chester I. Mead, 1930 Truxton Ave., Bakersfield.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Councill Rudolph, 103–5th St. S., St. Petersburg.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association convention and fall meeting.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Alton Johnson, 102 E. Central Ave., Valdosta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Place: Atlanta. Time: At time of annual state meeting.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB OF CONNECTICUT

President: Dr. David Gaberman, 1179 Allyn St., Hartford, Conn.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Matthew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.
Secretary-Treasurer: Dr. James Dunn, 414 Blackhawk Hotel, Davenport.

Louisiana State Pediatric Society

President: Dr. S. George Wolfe, 1560 Line Ave., Shreveport.
Secretary-Treasurer: Dr. W. C. Rivenbark, 1448 Louisiana Ave., New Orleans 15.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn, N. Y.
Secretary: Dr. George R. Murphy, 292 Madison Ave., New York.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Donald J. Barnes, 3001 W. Grand Blvd., Detroit, Mich.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.

Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

Nebraska Pediatric Society

President: Dr. John M. Thomas, 1418 Medical Arts Bldg., Omaha 2.
Secretary-Treasurer: Dr. Gerald C. O'Neil, 640 City National Bank Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

New Mexico State Pediatric Society

President: Dr. M. K. Wylder, 221 W. Central Ave., Albuquerque.
Secretary-Treasurer: Dr. Ly Werner, 221 W. Central Ave., Albuquerque.

North Carolina Pediatric Society

President: Dr. Charles R. Bugg, Professional Bldg., Raleigh.
Secretary: Dr. Charles F. Williams, 817 Hillsboro St., Raleigh.

Northern California Pediatric Society

President: Dr. Edith M. Meyers, 431–30th St., Oakland.
Secretary: Dr. A. L. Gleason, 411–29th St., Oakland 9.
Place: San Francisco. Time: Second Thursday of February, April, September and November.

Oklahoma State Pediatric Society

President: Dr. G. R. Russell, 604 S. Cincinnati Ave., Tulsa.
Secretary: Dr. Luverne Hays, 108 W. 6th St., Tulsa.
Place: With Oklahoma State Medical Association. Time: Annual Meeting.

South Carolina Pediatric Society

President: Dr. George D. Johnson, Spartanburg.
Secretary-Treasurer: Dr. B. O. Ravenel, Roper Hospital, Charleston.

Tennessee Pediatric Society

President: Dr. F. T. Mitchell, 376 S. Bellview, Memphis.
Secretary-Treasurer: Dr. W. O. Vaughan, 2103 Hayes St., Nashville 5.
Time: Second Monday in April.

Texas Pediatric Society

President: Dr. Max Woodward, 202 N. Travis St., Sherman.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas 4.

Virginia Pediatric Society

President: Dr. Emily Gardner, 1100 W. Franklin St., Richmond 20.
Secretary: Dr. Louise Galvin, 214 S. Boulevard, Richmond 21.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. Jack Basman, 1021 Quarrier St., Charleston.
Secretary: Dr. Harry E. Baldock, Medical Arts Bldg., Charleston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. I. Hartman, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. Alexander N. Freed, 2012 W. 25th St., Cleveland.
Place: Cleveland Medical Library Bldg. Time: 8:15 p. m., October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. J. H. Ebbs, 13 Queen's Park, Toronto, Canada.
Secretary: Dr. J. F. McCreary, 170 St. George St., Toronto, Canada.
Place: Academy of Medicine. Time: 8:30 p. m., third Thursday of each month.

Baltimore City Medical Society, Pediatric Section

Chairman: Dr. Charles O'Donovan Jr., 5 E. Read St., Baltimore.
Secretary: Dr. T. Campbell Goodwin, 16 E. Biddle St., Baltimore.

Bronx Pediatric Society

President: Dr. Walter Levy, 12 E. 88th St., New York.
Secretary: Dr. Joseph Blasenstein, 960 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Lambert Krahulik, 14 Sidney Pl., Brooklyn.
Secretary: Dr. Joseph Battaglia, 713 Bushwick Ave., Brooklyn 21.
Place: Granada Hotel. Time: 8:45 p. m., fourth Wednesday of February, March, April, May and November.

Buffalo Pediatric Society

President: Dr. Douglas P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo 9, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

Central New York Pediatric Club

President: Dr. Arthur W. Benson, 2 St. Paul St., Troy.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and October.

Chicago Pediatric Society

President: Dr. Joseph Greengard, 4753 Broadway, Chicago 40.
Secretary: Dr. Alvah L. Newcomb, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May inclusive.

Cincinnati Pediatric Society

President: Dr. Leo S. Friedman, 666 Rockdale Ave., Cincinnati 29.
Secretary: Dr. George Renner, 3144 Jefferson Ave., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. O. René Caillet, 4325 Cole Ave., Dallas, Texas.
Secretary-Treasurer: Dorothy Wyvell, Bradford Memorial Hospital for Babies, Texas.
Place: Children's Medical Center. Time: 1 p. m., third Saturday and 8:30 p. m., the first Thursday of each month.

Detroit Pediatric Society

President: Dr. Otto Grob, 651 Fisher Bldg., Detroit 2, Mich.
Secretary: Dr. Harold B. Rothbart, 773 Fisher Bldg., Detroit 2, Mich.
Place: Variable. Time: Third Wednesday of each month.

Houston Pediatric Society

President: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: River Oaks Country Club. Time: 7:30 p. m., fourth Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1624 Professional Bldg., Kansas City.
Secretary: Dr. Leland Speer, 1022 Parkway, Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Albert L. Hill, 1401 S. Hope St., Los Angeles.
Secretary-Treasurer: Dr. Robert Simonds, 1925 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Henry Rascoff, 895 Eastern Parkway, Brooklyn.
Secretary: Dr. Harold Levy, 750 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Meyeron Coe, 217-02–91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Louis Appel, 143-42 Cherry Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. John Washington, 2203 Wyoming Ave., Washington, D. C.
Secretary-Treasurer: Dr. George Maksim, 1418 Good Hope Rd. S.E., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., third Thursday of October, January, March and May.

Memphis Pediatric Society

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Barton Etter, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis Country Club. Time: 8 p. m., Dec. 13, 1946.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. R. P. Showalter, 411 E. Mason St., Milwaukee 2.
Place: Milwaukee Children's Hospital. Time: Second Wednesday in February, April, June, October and December.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Robert O. Du Bois, 122 E. 76th St., New York.
Secretary: Dr. Harold W. Dargeon, 1095 Park Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from November to May, inclusive, 8:30 p. m.

Oklahoma City Pediatric Society

President: Dr. William M. Taylor, 625½ N. W. 10th St., Oklahoma City.
Secretary: Dr. Jeanne McKinnon-Shofstall, 1019 N. Lee St., Oklahoma City.
Place: Oklahoma Club. Time: Third Thursday of each month.

Philadelphia Pediatric Society

President: Dr. Waldo E. Nelson, Temple University School of Medicine, Philadelphia.
Secretary: Dr. Sherman Little, 1740 Bainbridge St., Philadelphia 46.
Place: College of Physicians, 19 S. 22d St. Time: 8:30 p. m., second Tuesday in October, December, February and April.

Pittsburgh Pediatric Society

President: Dr. Elwood Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh 13.
Place: Pittsburgh Academy of Medicine. Time: Second Friday in October, December, February and April.

Richmond Pediatric Society

President: Dr. Edwin L. Kendig Jr., 828 W. Franklin St., Richmond 20, Va.
Secretary-Treasurer: Dr. Thomas S. Chalkley, 1200 E. Broad St., Richmond, Va.
Place: Medical College Hospital. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. William L. Bradford, 260 Crittenden Blvd., Rochester 7, N. Y.
Secretary-Treasurer: Dr. Donald D. Posson, 222 Chili Ave., Rochester 11, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee.
Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Joseph C. Jaudon, 337 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Gilbert B. Forbes, 500 S. Kingshighway, St. Louis 10.
Time: Second Thursday of each month from October to May, inclusive.

Seattle Pediatric Society

President: Dr. Norman W. Murphy, 1300 Madison St., Seattle 4.
Secretary: Dr. David M. Harris, 630 Medical Arts Bldg., Seattle 1.
Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Robert J. Dostal, 710 Wilshire Blvd., Santa Monica, Calif.
Secretary: Dr. H. M. Van Dyke, 541 E. Broadway, Long Beach, Calif.
Place: University Club of Los Angeles. Time: 6:30 p. m., first Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Park Bradshaw, Muskegon, Mich.
Secretary: Dr. Harry A. Towsley, 1313 E. Ann St., Ann Arbor, Mich.
Place: University Hospital, Ann Arbor, Mich. Time: Oct. 25-26, 1946.

Westchester County Medical Society, Pediatrics Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.
Place: Hospitals of Westchester County. Time: Third Thursday in November, January, March and May.